Section for
General Practitioners Included

Antibiotic Guidelines

6th Edition, 1990/91

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ANTIBIOTIC GUIDELINES

6th Edition, January 1990

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NOTES ON THE USE OF THESE GUIDELINES

1. The regimens given in the text apply to average sized, non-pregnant adults.
2. Paediatric doses will be found in the table on p. 115-119.
3. Special consideration should be given to the following:
   a. Safety in pregnant and lactating women and in children.
   b. Need to monitor antimicrobial levels, e.g. aminoglycosides, vancomycin and in neonates, chloramphenicol (see p. 113).
   c. Dosage adjustment in renal or hepatic impairment and in the elderly.

In complicated situations these Guidelines are no substitute for consultation with a practitioner experienced in the management of a particular infection.

These guidelines do not include important information such as contraindications, precautions and adverse effects relevant to the various antimicrobial agents recommended.

RESPONSIBLE USE THEREFORE REQUIRES THAT THE PRESCRIBER IS FAMILIAR WITH THE ABOVE.

SPECIFIC DRUG INFORMATION

Further information relating to drugs may be obtained from Departments of Clinical Pharmacology, Hospital Pharmacies, and State Drug Information Centres, telephone: (03) 342 7777 (Vic), (02) 553 2361 (NSW), (08) 275 9301 (SA), (07) 253 7098 (Qld), (002) 38 8737 (Tas), (09) 389 2923 (WA), (089) 20 8424 (NT), (062) 43 2113 (ACT).

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PREFACE

This 6th edition of *Antibiotic Guidelines* marks the emergence of the publication as a truly National document. The last edition was endorsed by the health authorities of South Australia, Queensland, New South Wales and Victoria. They have now been joined by Tasmania, Western Australia and the Northern Territory. The booklet has thus been accepted by every State in the Commonwealth and by the largest Territory.

This edition has been thoroughly revised by the various writing groups and each recommendation can be regarded as current at the time of publication. Several changes will be noticed such as:

- a complete revision of the section on infections of the genital tract which now forms a separate chapter;
- prophylactic regimens for endoscopic procedures have now been included;
- recommendation of trimethoprim in place of co-trimoxazole in many situations where evidence exists for efficacy of the former;
- reduction of dose frequency for oral penicillin and erythromycin in upper respiratory tract infections;
- some increase in the recommendation of third generation cephalosporins;
- the appearance of quinolones in the few situations where they represent cost-effective therapy.

The original aim of the guidelines was to provide advice on effective, safe and economical use of antibiotics in hospital. Its ever increasing acceptance implies that this has been successfully achieved. It must be borne in mind that the

recommendations are not proscriptive and that 100% concordance of practice with them is not to be expected; however a prescriber should have reasons for deviating from them. However the 5th edition attempted to widen its audience by including a section directed to community practice. This was simply a collection of those recommendations that seemed particularly relevant to the general practitioner. In this edition the text of this section has been modified in many places to encompass special circumstances, such as the frequency of undifferentiated presentations which do not permit the sort of precise diagnoses on which regimens are based in the main body of the text.

These attempts to increase the relevance of the section have been assisted greatly by a project conducted in Victoria to encourage use of Antibiotic Guidelines recommendations in the treatment of tonsillitis. Several hundred general practitioners generously cooperated in an audit of prescribing behaviour and were visited by an "academic detailer". It is hoped that this section of the book will increasingly provide the type of benchmark statement for the general practitioner which the main text does for hospital antibiotic use. This will furnish the basis for a mechanism of review of practice which in turn provides information valuable in producing succeeding editions.

Victorian Writing Group.

January 1990

Melbourne, Australia.

DEMOCRATIC MEDICAL ASSOCIATION

The Democratic Medical Association is a newly formed professional organisation of doctors that work for the objective of improving the health status of the people upholding the high academic standards and ethical values expected from the medical profession.

The manifesto of DMA discusses among other things the need for imparting the concept of rational drug use to the members of the medical profession. The manifesto says "In this age of knowledge explosion the academic standards of the doctors should be regularly updated. In the place of the promotional materials supplied by the drug companies the medical profession should be provided with independent and scientific drug information".

It is to realise this objective that DMA has decided to undertake the publication of books and pamphlets to disseminate scientific drug information. We are extremely happy to begin our venture with the publication of 'Antibiotic Guidelines' prepared by the Victorian Medical Postgraduate Foundation (Australia).

We express our sincere thanks and gratitude to Dr. Ken Harvey (Consultant Microbiologist, Victorian Medical Postgraduate Foundation Inc) and the Health Department of Victoria for giving us permission to publish this book.

Medical College Hospital,
Calicut
10th March 1990

Dr. B. Ekbal
Convener,
Publication Committee, DMA

CONTENTS

INTRODUCTION

Bacterial diseases remain a major cause of illness and death throughout the world despite five decades of antimicrobial use. In large part, this is due to social and economic factors including both poverty and technological advances fostering development of infection. However. there are increasing instances where the resistance to antimicrobials acquired by previously susceptible organisms is the cause of treatment failure or requires the use of larger doses or more expensive or toxic agents. This is dramatically exemplified by the problems with *Staphylococcus aureus, Neisseria gonorrhoeae,* and *Haemophilus influenzae* and the increasing resistance of bacteria as diverse as Enterobacteriaceae and *Streptococcus pneumoniae,* is harbinger of further problems to come.

It must be assumed that the use of antimicrobials is a major factor in the development of such resistance. Antimicrobials must therefore be regarded as environmentally hazardous; they are also a common cause of adverse reactions. These disadvantages dictate that antimicrobials be used in a rational and appropriate manner.

Unfortunately, surveys have shown that inappropriate antibiotic prescribing is widespread. One clinician's bad prescribing habits can directly affect patients of colleagues via selection of, and cross-infection by, antibiotic-resistant microorganisms. Furthermore, the profligate use of antimicrobials in one locality may result in resistant organisms with the potential to spread widely and rapidly.

This booklet is intended to provide a general statement of acceptable approaches to the use of antimicrobial drugs both in hospital practice and in the community. Within a given institution the choice of which drugs are used may be influenced by such local factors as trends in sensitivity of current isolates, cost of the drugs negotiated by the pharmacy and in some instances traditional preference or familiarity. The drug committee of each hospital should

produce its own antibiotic policy within the overall framework suggested by this booklet.

Recommendations for use of antimicrobial drugs in general practice have been collected in the coloured pages of the booklet. In the community, practitioners should examine their individual prescribing habits in the light of these suggested regimens.

HOSPITAL ANTIBIOTIC POLICIES

The importance of each hospital adhering to a defined antibiotic policy is internationally accepted. The aim is to minimise the selection of antibiotic-resistant microorganisms and promote effective, economical prescribing. Successful implementation of antibiotic policies requires that hospital drug committees should:

- formulate prescribing strategies appropriate for their institution
- audit antibiotic use
- organise appropriate educational measures, and
- recognise the forces influencing prescribing doctors.

Prescribing strategies

1. Hospitals should classify antimicrobial preparations into three groups: unrestricted, restricted and excluded. The primary aim of such policies is not to prevent access to useful drugs but rather to require doctors to justify their use of certain antibiotics and have their decisions subject to peer review.

   Unrestricted. No restrictions should be placed on antimicrobials which are safe, effective and relatively cheap, e.g. benzylpenicillin.

   Restricted. Drugs may be restricted because of concern regarding antimicrobial resistance, cost-containment or safety. Many degrees of restriction are possible: limited supplies available on one prescription, use only in defined situations, authority to prescribe limited to certain medical staff or special units, and supply only after consultation and approval from a medical microbiologist, infectious disease physician or other clinician nominated by an appropriate committee. A mechanism must exist whereby an initial dose of a restricted antibiotic can be given in an emergency, after which approval is sought.

   In most States and Territories, drugs to treat mycobacterial infections have their use restricted by regulations imposed by the

Health Authorities but they are supplied free of charge following notification of a case of tuberculosis.

Excluded. Agents in this category would include preparations considered to have no useful advantage over drugs already held, or drugs superseded by newer releases e.g. numerous penicillins, cephalosporins, tetracyclines and sulphonamides. These agents would not normally be stocked by a hospital pharmacy and would only be obtained for use under special circumstances. All new antimicrobial agents should be automatically placed in the excluded category until the appropriate hospital committee has considered their role in therapy.

A written request from a hospital clinician should be required before a drug is considered for reclassification by the appropriate committee. Suggestions as to which drugs should be restricted or excluded will be found in the section - "Comments on Selected Antimicrobials" (p. 5-12).

2. Hospital laboratories should limit the range of antibiotics for which sensitivity tests are reported routinely. Sensitivities to restricted antibiotics should only be reported if the organism isolated is resistant to non-restricted antibiotics. This does not imply that the antibiotics actually tested will be restricted but some results will be retained by the laboratory for reference if required.

3. Hospitals may rotate drugs or cease the use of a particular agent for a period of time if resistance is emerging rapidly and suitable alternatives are available.

Antibiotic audits

Reviews of antibiotic usage by product and by clinical unit, with occasional audits of prescribing habits, may suggest specific educational campaigns.

Educational responsibilities

Educational functions of hospital drug committees should include the provision of information on antibiotic use such as this booklet, supplemented by local decisions and data on new antibiotics as these become available. Drug committees should encourage the provision of information to clinicians on current antibiotic sensitivity patterns of organisms from various patient subgroups.

Forces influencing prescribing

Prescribing habits have been shown to be influenced by education, peer influences, physician characteristics, activities of the pharmaceutical industry such as advertising and drug detailing, control and regulatory measures, and demands from patients and society. It is the task of the hospital drug committee to augment influences that foster rational prescribing and to counter those that have the opposite effect.

PRINCIPLES OF ANTIBIOTIC USE

In making these recommendations, the following principles have been observed:

1. **Choice of an antimicrobial agent** should be based on factors such as spectrum of activity, anticipated efficacy, safety, previous clinical experience, cost, potential for selection of resistance and associated risk of superinfection. The relative importance of each of these factors will be influenced by the severity of the illness and whether the drug is to be used for prophylaxis, empirical therapy or therapy directed by identification of one or more pathogens.

2. **Prophylactic antimicrobial therapy** should be restricted to the use of a limited range of agents of proven efficacy in invasive procedures with a high risk of infection or where the consequences of infection are disastrous. Most surgical prophylaxis should be parenteral and commence just before the procedure, continuing for no more than one or two doses after the end of the operation. The aim is to achieve high plasma and tissue levels at the time that contamination is most likely, i.e. during the operation.

3. **Empirical antimicrobial therapy** should be based on local epidemiological data on potential pathogens and their patterns of antibiotic susceptibility. Appropriate specimens for Gram stain, culture and sensitivity testing should be obtained before commencing antimicrobial therapy. A Gram stain (e.g. of spinal fluid or sputum) or direct antigen detection methods (e.g. in meningitis) may allow specific therapy even before the pathogen has been cultured.

4. **Directed antimicrobial therapy** for proven pathogens should include the most effective, least toxic, narrowest spectrum agent available. This practice reduces the problems associated with broad-spectrum therapy, viz. selection of resistant microorganisms and superinfection.

5. **Choice of parenteral, oral or topical antimicrobial formulations** should be determined by the site and severity of infection. Intravenous therapy via a central line may be necessary to avoid causing phlebitis when an irritant concentration of a drug is administered. It is important that topical antimicrobial therapy be restricted to a few proven indications, e.g. eye infections because of the capacity of most topical agents to select resistant microorganisms and to cause sensitisation; topical antiseptics are to be preferred in most situations.

6. **Antimicrobial combinations** have few indications. These include:
   (i) to extend the spectrum of cover, e.g. in empirical therapy or in mixed infections,
   (ii) to achieve a more rapid and complete bactericidal effect (synergy), e.g. in enterococcal endocarditis, or
   (iii) to prevent the emergence of resistant microorganisms, e.g. in the therapy of tuberculosis.

COMMENTS ON SELECTED ANTIMICROBIALS

Most conditions requiring antimicrobial treatment can be managed using old and established drugs. This is reflected in the recommendations made in the body of this booklet. The beta-lactams and the aminoglycosides are two important groups of antimicrobials used extensively in hospitals. These drugs have been difficult to understand because of their number and the claims often made for them. Newer examples of these groups are usually expensive but may be valuable in treating resistant nosocomial infections. Paradoxically their use may unfortunately be a factor in the selection of resistant organisms.

BETA-LACTAMS

Penicillins, cephalosporins (here used to include cephamycins), monobactams and the carbapenem, imipenem, are structurally related and share bactericidal activity primarily directed at the bacterial cell wall. The beta-lactamase inhibitors, clavulanic acid and sulbactam, have little intrinsic antibacterial activity against most organisms but, when combined with other beta-lactam drugs susceptible to enzymatic inactivation (e.g. amoxycillin and ticarcillin), extend their useful spectrum.

Most beta-lactams are relatively safe, except in those patients hypersensitive to them.

Penicillins

Narrow spectrum

These are mainly active against Gram-positive organisms but are inactivated by staphylococcal beta-lactamase.

1. Benzylpenicillin (penicillin G) is administered parenterally. It remains the treatment of choice for many infections.
2. Procaine penicillin is an intramuscular preparation designed to extend the half-life of benzylpenicillin but only provides adequate levels for up to 24 hours against highly susceptible organisms.
3. Benzathine penicillin is given intramuscularly and provides low levels of benzypenicillin for up to 4 weeks.
4. Phenoxymethylpenicillin (penicillin V) which differs chemically from benzylpenicillin, is acid stable and thus may be given orally, although food impairs absorption. It is intrinsically less active than benzylpenicillin.

Antistaphylococcal

Methicillin, cloxacillin and flucloxacillin are stable to staphylococcal beta-lactamase. They are microbiologically similar but because of greater toxicity, methicillin should be replaced by cloxacillin or flucloxacillin. Flucloxacillin is more reliably absorbed by the oral route than is cloxacillin and it may cause less gastrointestinal upset. The microbiological activities of these two products are similar and thus the parenteral form of flucloxacillin offers no special advantage

over cloxacillin. In this booklet (flu)cloxacillin refers to either product. Hospitals should only stock one member of this group for each route of administration. Methicillin-resistant *Staphylococcus aureus* (MRSA) should be regarded as clinically resistant to all beta-lactams irrespective of laboratory reports of sensitivity.

Broad Spectrum (aminopenicillins)

Ampicillin, and amoxycillin have greater activity than benzylpenicillin against some Gram-negative organisms (e.g. *E. coli, H. influenzae*) but are destroyed by beta-lactamase producing strains. They are agents of choice against enterococci. Amoxycillin is better absorbed than ampicillin but when given parenterally they are equivalent. In this booklet they are usually recommended interchangeably as (amoxy)ampicillin.

Antipseudomonal

Ticarcillin has replaced the less active carbenicillin. Mezlocillin is roughly equivalent to ticarcillin by in-vitro testing but azlocillin and piperacillin appear more active, especially against Klebsiella and Pseudomonas species. However, results with the latter two drugs vary with inoculum size and also depend upon whether bacteriostatic or bactericidal end points are used. The clinical importance of these findings is not yet established. The ureidopenicillins, azlocillin and piperacillin should not generally replace ticarcillin until such time as superior cost-benefit has been established.

Beta-Lactamase Inhibitors

Clavulanic acid and sulbactam are beta-lactamase inhibitors that inhibit the enzymes produced by *Staphylococcus aureus, B. fragilis* and also the ubiquitous TEM enzyme (found in *E. coli, N. gonorrhoeae* and *H. influenzae*) . They possess little antibacterial activity themselves, but in combination with penicillins such as amoxycillin, they can preserve the usefulness of such drugs and extend their spectrum of activity. These combinations should be reserved for the treatment of organisms in which resistance to the beta-lactam antibiotic component is due to enzymes which these new agents can inhibit.

Carbapenems

Imipenem is the only available member of this class. It is inactivated by a renal dipeptidase and is therefore formulated in combination with the dipeptidase inhibitor, cilastatin. This preparation has activity against Enterobacteriaceae and *Pseudomonas aeruginosa* comparable to that of aminoglycosides and in addition has excellent activity against anaerobes, including *B. fragilis* and most Gram-positive cocci. However it does not reliably cover MRSA nor is it active against some strains of Pseudomonas species.

Monobactams

Aztreonam is a member of this novel family of beta-lactams. This compound is relatively inactive against Gram-positive organisms and anaerobes but is highly active against the majority of aerobic Gram-negative bacteria, including beta-lactamase producing *H. influenzae*, Enterobacteriaceae and Pseudomonas species including those resistant to aminoglycosides.

Cephalosporins and Related Drugs

The early cephalosporins available for clinical use were rarely regarded as drugs of first choice by infectious disease physicians and microbiologists. This was not because of lack of efficacy or concern about toxicity, but rather because other antibiotics were already established and cephalosporins usually provided no clear advantage and invariably cost more. However, such opinion had little impact on their widespread use, especially in Japan and the USA. More recent cephalosporins have more specific indications and may sometimes be the drug of first choice, albeit in uncommon situations.

Cephalosporins may be used, with due precautions in the penicillin hypersensitive patient, bearing in mind the small risk of cross-sensitisation (3 to 6%).

First Generation Drugs

cephalothin / cephazolin
cephalexin / cefaclor

The microbiological spectra of these agents are similar but there are differences in the routes of administration. Cephalothin, the prototype cephalosporin, can be likened to a combination of cloxacillin and

ampicillin. It is active against penicillinase-producing Staphylococci and its Gram-negative spectrum includes *E. coli* and Klebsiella species among the Enterobacteriaceae.

However, unlike ampicillin, cephalothin is not active against *Enterococcus faecalis* and is much less active against *H. influenzae*. No first generation cephalosporin has useful activity against the Gram-negative anaerobe, *Bacteroides fragilis*, nor against Gram-negative aerobic bacteria such as Serratia, Enterobacter or Pseudomonas. Cephazolin can be regarded as similar to cephalothin but is more suitable for intramuscular use.

Cephalexin and cefaclor can be given orally. Cefaclor has useful activity against *H. influenzae*.

Second Generation Drugs

cephamandole / cefoxitin

Drugs of this group are more stable to Gram-negative beta-lactamases and have an extended spectrum of activity against organisms such as Proteus, Citrobacter and Enterobacter, when compared to drugs of the first generation. Conversely, they are less active against Gram-positive organisms. Cefoxitin has greater activity than cephamandole against *B. fragilis* (60 to 70% of strains have been reported to be sensitive). However, these drugs have a limited role in therapy.

Cefoxitin has been used as a prophylactic antibiotic for bowel or gynaecological surgery. However, the anaerobic cover provided by imidazole compounds, such as metronidazole, is superior to that of cefoxitin.

Third Generation Drugs

cefotaxime / ceftriaxone
ceftazidime

These compounds have an extended spectrum of activity covering virtually all the Enterobacteriaceae. Ceftazidime is the only agent with predictable antipseudomonal activity. The activity of these drugs against *B. fragilis* varies, but none appear as active as cefoxitin. Third generation cephalosporins are less active against Gram-positive organisms than earlier generations. None has clinically useful activity against *Enterococcus faecalis* or MRSA. Unlike earlier cephalosporins, which do not enter the cerebrospinal fluid (CSF) in therapeutically useful concentrations, several third generation drugs

have been effective in Gram-negative meningitis because of better penetration and higher intrinsic activity. Ceftriaxone, has a considerably longer half-life than other members of this group.

Many later cephalosporins which are stable to beta-lactamases can paradoxically induce resistance which emerges during treatment. The organisms involved have been primarily *Pseudomonas aeruginosa*, as well as some strains of Serratia, Citrobacter and Enterobacter which then also exhibit resistance to most other beta-lactam drugs.

All third generation cephalosporins are expensive (10 to 20 times the cost of gentamicin) and it seems sensible to restrict their use.

AMINOGLYCOSIDES

streptomycin / gentamicin
tobramycin / netilmicin / amikacin

Different aminoglycoside antibiotics are preferable in specific clinical situations.

Streptomycin has a role in the treatment of pulmonary infection or meningitis due to *Mycobacterium tuberculosis*.

Gentamicin has a wide Gram-negative spectrum including *Pseudomonas aeruginosa* and is the aminoglycoside of choice for most cases of hospital-acquired aerobic Gram-negative sepsis.

Tobramycin is marginally more active *in vitro* than gentamicin against *Pseudomonas aeruginosa* (but not other aerobic Gram-negative bacteria) and is inactivated by a similar range of modifying enzymes. It is several times as expensive as gentamicin.

Netilmicin is more resistant to degradation by aminoglycoside-inactivating enzymes than gentamicin and tobramycin, but is less resistant than amikacin. It is claimed to be less ototoxic and nephrotoxic than gentamicin and tobramycin, although in practice, if therapy is monitored by rapid aminoglycoside assays, this virtue is seldom clinically apparent. Netilmicin is as expensive as tobramycin.

Amikacin remains the most resistant aminoglycoside to enzymatic inactivation, although resistant strains do occur. It is about twenty times as expensive as gentamicin.

Strategies of aminoglycoside use should depend on local sensitivity patterns. Where approximately 95% or more of aerobic Gram-negative isolates remain sensitive to gentamicin, this drug remains the aminoglycoside of choice, even for the empirical treatment of hospital-acquired sepsis. Tobramycin should be restricted and may have a role in treatment of suspected or proven Pseudomonas sepsis.

Netilmicin should be restricted to treatment of infections due to gentamicin/tobramycin-resistant microorganisms, or for use in patients where nephro- or ototoxicity is of particular concern. Amikacin must be reserved for treating infections due to microorganisms that are resistant to other aminoglycosides.

SULPHONAMIDES AND TRIMETHOPRIM

Sulphonamides now have limited use. Sulphamethoxazole in co-trimoxazole, the combined formulation with the dihydrofolate reductase inhibitor trimethoprim, has found widespread use as a broad-spectrum agent used particularly in respiratory and urinary tract infections. This was based on the theoretical advantages of inhibiting sequential steps in bacterial synthesis of folate derived co-factors and the *in vitro* demonstration of some degree of synergy between the two components. Clinical experience over many years has demonstrated the efficacy of the combined preparation. However there are several problems which question the use of this formulation. There are many reports of adverse effects, many of which are typical of those seen with sulphonamides and some of which are serious and even fatal, especially in the elderly. Rational use of the combination would require that the combination were associated with superior efficacy or decreased emergence of resistant organisms compared with trimethoprim alone. In most situations there are no data to support or refute these propositions.

QUINOLINE CARBOXYLIC ACID DERIVATIVES (QUINOLONES)

nalidixic acid
norfloxacin / enoxacin / ciprofloxacin

Nalidixic acid has been used primarily in the treatment of urinary infections and is no longer recommended. Norfloxacin has been approved for urinary and gastrointestinal infections.

Newer members of this group have a wide range of therapeutic activity including infections due to some Gram-positive cocci, Gram-negative cocci, many Gram-negative bacilli including *Haemophilus influenzae*, members of the Enterobacteriaceae, *Pseudomonas aeruginosa* and various species of Mycobacteria. Some of these compounds can be administered by the parenteral as well as the oral route and can be used to treat serious systemic infections. They are

however expensive and their full spectrum of adverse effects has probably not been elucidated. They are contraindicated for use in children less than 14 years of age because they cause damage to the joints of immature animals. They should be reserved for treatment of infection resistant to cheaper agents.

ANTIVIRAL AGENTS

Compounds with limited antiviral activity have been available for some time.

Idoxuridine found a place in the topical treatment of herpes infections although it was really only effective in dendritic corneal ulcers.

Vidarabine had some efficacy in herpes encephalitis and other serious herpetic diseases and is still available for herpetic keratitis.

Amantadine is used to a limited extent for Influenza A prophylaxis or early treatment.

Acyclovir is the first systemic antiviral with minimal toxicity. It is active against Herpes Simplex Virus and to a lesser extent Varicella-Zoster Virus and Epstein-Barr Virus. It is converted to the active metabolite only in cells infected with these viruses. Acyclovir has virtually replaced other antiherpetic drugs and has found an important place in the treatment and prevention of serious Herpes simplex and Varicella-Zoster infections. It is adminstered orally for severe primary skin infections, intravenously for herpes encephalitis and in the immunocompromised host and topically for herpes keratitis.

Ganciclovir (dihydroxy-propoxymethylguanine, DHPG) is currently being studied as a potential treatment for serious Cytomegalovirus infections in immunocompromised patients. Unfortunately, it has dose-dependent bone marrow suppressive effects.

Zidovudine (azidothymidine, AZT), a reverse transcriptase inhibitor, has been shown to prolong life and well-being in moderate to severe Human Immunodeficiency Virus infections. Anaemia is a common complication.

Ribavirin is an investigational agent with a broad antiviral spectrum. Its use is currently limited to life-threatening Respiratory Syncytial Virus infection and Lassa Fever.

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RESPIRATORY TRACT INFECTIONS

UPPER RESPIRATORY TRACT INFECTIONS

The majority of upper respiratory tract infections are viral in origin and antibiotics are not indicated.

ACUTE SORE THROAT

This is most often caused by viral infection. Diphtheria is now uncommon in Australia. If *Streptococcus pyogenes* infection is proven or suspected

phenoxymethylpenicillin		500 mg orally, 12-hourly for 10 days
	or	25 to 50 mg/kg/day in 2 or 3 divided doses for 10 days (to a maximum daily dose 1 g)

OR

erythromycin		500 mg orally, 12-hourly for 10 days
	or	25 to 50 mg/kg/day in 2 or 3 divided doses for 10 days (to a maximum daily dose of 1 g)

Although symptoms and most evidence of this infection will disappear within 1 or 2 days of treatment, a full course of 10 days should be prescribed to give the best chance of eradicating *Streptococcus pyogenes* from the nasopharynx and thereby minimising the risk of recurrence or complications such as glomerulonephritis or rheumatic fever. Treatment may be initiated with one injection of procaine penicillin intramuscularly. In severe disease, parenteral penicillin may be required for the initial 3 to 5 days and even longer in the treatment of quinsy.

Ampicillin or amoxycillin alone, or in combination with potassium clavulanate, SHOULD NOT BE USED as they have no

advantage over penicillin and more commonly produce a rash, especially if the sore throat is due to glandular fever (infectious mononucleosis).

ACUTE BACTERIAL OTITIS MEDIA AND SINUSITIS

Many children with viral upper respiratory tract infections have mild reddening or dullness of the ear drum and antibiotics are not warranted. In contrast, where the ear drum is red or yellow and bulging, with loss of anatomical landmarks, antibiotic therapy is indicated. Controlled trials have demonstrated no benefit from the use of decongestants or antihistamines but have noted more adverse experiences such as sleep disturbance, irritability, bad temper and hallucination. Their use is not recommended.

Common causative bacteria: *Streptococcus pneumoniae, Haemophilus influenzae. Branhamella catarrhalis* is less frequently isolated but is often amoxycillin-resistant. *Staphylococcus aureus* or anaerobes may less frequently be involved in acute sinusitis. However, the clinical outcome does not necessarily reflect *in vitro* susceptibility.

amoxycillin 750 mg orally, 12-hourly for 5 days
or 500 mg orally, 8-hourly for 5 days
or 25 to 50 mg/kg/day in 2 or 3 divided doses for 5 days (to a maximum daily dose of 1.5 g)

OR

trimethoprim 300 mg orally, 12-hourly for 5 days
In the absence of a paediatric suspension, co-trimoxazole may be substituted at a dosage of 6/30 mg/kg/day in 2 divided doses.

OR

doxycycline 100 mg orally, 12-hourly for 5 days. For milder infections 100 mg orally, once daily may suffice. Do not use doxycycline in children

OR

cefaclor 250 mg orally, 8-hourly for 5 days
or 20 to 40 mg/kg/day in 3 divided doses for 5 days (to a maximum daily dose of 1 g)

OR

amoxycillin/potassium clavulanate 500mg/125mg orally, 8-hourly for 5 days. This combination should not be preferred to

amoxycillin alone unless resistance to amoxycillin is suspected or proven

ACUTE EPIGLOTTITIS

A life-threatening cause of upper airway obstruction which is seen mainly in children but may occur in adults. Urgent hospitalisation is required. Commonly due to *Haemophilus influenzae* type b.

ceftriaxone 100 mg/kg to a maximum of 2 g/day intravenously, as a single daily dose
OR
cefotaxime 100 to 150 mg/kg/day to a maximum of 4 g/day intravenously, in 3 divided doses
OR
chloramphenicol 80 mg/kg/day initially intravenously, to a maximum of 4 g in 4 divided doses for 5 to 10 days

Chloramphenicol can be reliably administered by the oral route when the patient's condition has stabilised. The same is not true for ceftriaxone and cefotaxime.

If the organism is shown to be sensitive to (amoxy)ampicillin, this drug should be substituted for chloramphenicol. If chloramphenicol resistance is known or suspected, a third generation cephalosporin may be used e.g.,

cefotaxime 100 to 150 mg/kg/day intravenously, in 3 divided doses

ACUTE BRONCHITIS

In a previously healthy person, acute bronchitis is most often viral. If severe, secondary bacterial infection may be assumed, usually due to *Streptococcus pneumoniae* or *Haemophilus influenzae*.

amoxycillin 750 mg orally, 12-hourly for 5 days
or 500 mg orally, 8-hourly for 5 days
OR
doxycycline 200 mg orally, as a loading dose, then 100 mg orally, daily for 5 days
OR
erythromycin 500 mg orally, 8-hourly for 5 days

If *Mycoplasma pneumoniae* infection is suspected on epidemiological grounds, amoxycillin is inappropriate.

ACUTE EXACERBATIONS OF CHRONIC BRONCHITIS

While these are commonly viral in origin, important causative bacteria are: *Streptococcus pneumoniae* and *Haemophilus influenzae; Branhamella catarrhalis* is less frequently involved and is commonly amoxycillin resistant. Clinical outcome is not necessarily predicted by *in vitro* sensitivity.

amoxycillin 750 mg orally, 12-hourly for 5 days
or 500 mg orally, 8-hourly for 5 days
OR
trimethoprim 300 mg orally, 12-hourly for 5 days
OR
doxycycline 100 mg orally, 12-hourly for 5 days
OR
erythromycin 500 mg orally, 8-hourly for 5 days
OR
amoxycillin/potassium clavulanate 500 mg/125 mg orally, 8-hourly for 5 days. This combination should not be preferred to amoxycillin alone unless resistance to amoxycillin is proven or suspected because of lack of response or recurrence.

INFLUENZA

Antibiotics are not indicated in a previously healthy person. In those at special risk (e.g. chronic heart or lung disease, the elderly or pregnant women), secondary bacterial infection may require treatment as for acute bronchitis (see p. 16).

PNEUMONIA

Treatment will frequently have to be initiated for a patient with the clinical and X-ray features of pneumonia before a bacteriological diagnosis can be confirmed and therapy modified as appropriate. If the clinical response to parenteral therapy is satisfactory, high dose oral therapy may be substituted after a few days.

Pneumonia in previously healthy adults and children

The predominant bacterial pathogen is *Streptococcus pneumoniae.*

benzylpenicillin 600 mg intravenously, 4 to 6-hourly for 5 to 10 days *(moderate to severe disease)*
OR (for mild disease only)
procaine penicillin 1.5 g intramuscularly, daily for 5 days
OR (for mild disease only)
as for acute exacerbations of chronic bronchitis (see p. 17)

In patients hypersensitive to penicillin, erythromycin may be used as in the regimen given for **Atypical Pneumonia** (see below).

A proportion of cases may be caused by *Haemophilus influenzae.* However, the tissue concentrations of benzylpenicillin produced by the above regimens are adequate to deal with most strains of *H. influenzae* and the practice of combining intravenous penicillin with (amoxy)ampicillin, or using intravenous (amoxy)ampicillin alone, is not recommended. However, if after initial parenteral treatment it is planned to continue with oral administration, phenoxymethylpenicillin will be unsatisfactory to cover *H. influenzae,* so amoxycillin or trimethoprim should be used (see doses under acute exacerbations of chronic bronchitis, p. 17). If *Staphylococcus aureus* is suspected or proven, flucloxacillin should be used (see Staphylococcal pneumonia p. 20).

"Atypical" pneumonia

May be seen in Mycoplasma and Legionella infections, Psittacosis or Q fever. Often occurs in previously healthy subjects.

doxycycline 100 mg orally, (or if severe, intravenously), 12-hourly for 7 to 10 days (Recommended for Psittacosis or Q fever, satisfactory for Mycoplasma)
OR
erythromycin 500 mg orally, 6-hourly for 7 to 10 days. If severe, commence with erythromycin 0.5 to 1 g, intravenously, 6-hourly (Recommended for Legionella infection, satisfactory for Mycoplasma)

Pneumonia in infancy (excluding neonates)

Most cases are viral, but a possible bacterial cause must be assumed because such an infection may be life-threatening. Antibiotics should cover *Streptococcus pneumoniae, Haemophilus influenzae* and *Staphylococcus aureus*. If the infection is overwhelming, treat as for acute epiglottitis (see p. 16), otherwise

(amoxy)ampicillin 25 to 75 mg/kg/day intravenously, in 4 divided doses for 7 to 10 days
TOGETHER WITH
(flu)cloxacillin 50 to 100 mg/kg/day intravenously, in 4 divided doses for 7 to 10 days
OR (AS A SINGLE AGENT)
erythromycin 25 to 50 mg/kg/day intravenously or orally, in 3 or 4 divided doses for 7 to 10 days, (especially for chlamydial or mycoplasma pneumonia)

Pneumonia developing in hospital or in patients with lowered resistance including immunosuppression

Common causative bacteria: *Streptococcus pneumoniae, Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa.*

Organism not yet known

benzylpenicillin 0.6 to 1.2 g intravenously, 4 to 6-hourly
TOGETHER WITH
gentamicin 2 mg/kg intravenously, as a loading dose then 1 to 1.5 mg/kg intravenously, 8-hourly each for 7 to 10 days or until bacteriology is clarified

This combination may be replaced by cefotaxime or ceftriaxone in elderly patients or those with renal impairment (see under Septicaemia p. 50).

If there is a high incidence of organisms resistant to these antibiotics in a particular unit or institution, then a different regimen, using reserve antibiotics, may need to be considered after appropriate microbiological consultation. Failure to control the infection should lead to re-evaluation of the antibiotic therapy.

If an organism is isolated which proves sensitive to penicillin, then benzylpenicillin alone is the drug of choice.

If a patient with pneumonia is hypersensitive to penicillin, a cephalosporin (e.g. cephalothin 1 to 2 g intravenously, 4 to 6-hourly) can be used, with due caution, bearing in mind that 3% to 6% of patients with penicillin hypersensitivity will also cross-react to cephalosporins. If the patient's history of penicillin hypersensitivity is such that even this risk is unacceptable

vancomycin 1 g intravenously, 12-hourly infused over at least 1 hour
OR
erythromycin 1 g intravenously, 6-hourly

can be substituted for benzylpenicillin in the above regimen.

Staphylococcal pneumonia (suspected on clinical or radiological grounds)

Substitute (flu)cloxacillin 1 to 2 g intravenously, 4-hourly for benzylpenicillin in the above regimen for "Organism not yet known" and discontinue gentamicin if *Staphylococcus aureus* is proven.

Patients with pneumonia suspected or proven to be due to MRSA should be treated initially with

vancomycin 1 g intravenously, 12-hourly, infused over at least 1 hour

These patients should be nursed in isolation. Consultation should be sought on the timing and type of subsequent oral therapy.

Fungal, viral or other pneumonia

e.g. *Candida albicans, Aspergillus fumigatus, Pneumocystis carinii,* or viruses such as *Cytomegalovirus* occur particularly in patients immunosuppressed following treatment with corticosteroids or cytotoxic drugs or in *Human Immunodeficiency Virus* (HIV) infection. Due to the wide range of possibilities, a clinical microbiologist or infectious disease physician should be consulted. Bronchoscopy and/or open lung biopsy may be necessary to establish a specific diagnosis.

Pneumocystis carinii pneumonia may be treated with:

co-trimoxazole (trimethoprim 20 mg/kg/day, sulphamethoxazole 100 mg/kg/day) orally or intravenously, in 4 divided doses for 2 to 3 weeks (preferred treatment)
OR
pentamidine isethionate* 4 mg/kg/day, as a single dose intravenously, diluted in 5% dextrose infused over 2 hours, for 14 days (if unsatisfactory response to co-trimoxazole)

Aspiration pneumonia and lung abscess

Streptococcus milleri and anaerobes are the major causative organisms. *Staphylococcus aureus* and Gram negative bacilli (e.g. *Klebsiella pneumoniae*) may be involved in a small number of cases.

benzylpenicillin 600 mg intravenously, 4 to 6-hourly for 10 to 14 days
TOGETHER WITH
metronidazole 500 mg intravenously, 12-hourly (infused over 20 minutes) initially for 1 to 2 days, then 200 to 500 mg orally, 8-hourly or 1 g rectally, 8-hourly for 10 to 14 days
OR (AS A SINGLE AGENT)
clindamycin 600 mg intravenously, 8-hourly (diluted in 100 ml and infused over at least 30 minutes), then 150 to 300 mg orally, 6-hourly for 10 to 14 days

If infection with aerobic Gram-negative bacilli or *Staphylococcus aureus* is suspected or proven.

gentamicin 2 mg/kg intravenously, as a loading dose then 1.5 mg/kg intravenously, 8-hourly for the Gram-negative bacilli or (flu)cloxacillin 1 to 2 g intravenously, 4-hourly for *Staphylococcus aureus*

should be added or substituted as appropriate.

For uncomplicated aspiration pneumonia, 10 days therapy will usually prove adequate, but where there is extensive disease or abscess formation, more prolonged high dose therapy may be required.

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* Available in Australia only to designated treatment centres, or on an Individual Patient Use basis through the Commonwealth Department of Health.

Tuberculous pneumonia

Multiple drug therapy is initiated primarily to guard against the existence and/or emergence of resistant organisms. It is appropriate to commence treatment with three drugs, as specified below, unless the patient has acquired the infection in an area such as S. E. Asia where there is known to be a high incidence of drug-resistant organisms. In these circumstances, a four drug regimen must be employed pending adequate sensitivity studies.

For many years, initial therapy has consisted of rifampicin and isoniazid together with either ethambutol and/or streptomycin. In recent years, pyrazinamide has replaced ethambutol because of its ability to destroy mycobacteria within macrophages and thereby shorten the duration of treatment. Ethambutol remains useful as a fourth drug in patients suspected of having isoniazid-resistant organisms.

In the presence of known or suspected hepatic disease, considerable care is needed in the initiation of chemotherapy, and it is prudent to space the introduction of rifampicin and isoniazid by 7 to 10 days, depending on liver function tests and the patient's general response.

Tuberculosis is a notifiable disease and must be reported to State Health Departments from whom advice is also available. Therapy should be reviewed when sensitivity results are available or in the event of adverse experiences to the drugs. For chemoprophylaxis see p. 68.

Short course therapy, 6 month duration (3 drugs)

rifampicin 10 mg/kg/day (to a maximum daily dose of 600 mg) orally, once daily
PLUS
isoniazid 10 mg/kg/day (to a maximum daily dose of 300 mg) orally, once daily
PLUS
pyrazinamide 30 mg/kg/day (to a maximum daily dose of 2 g) orally, once daily

Three drug therapy should continue for a minimum 2 months, at which time susceptibility results should be available. If the organism proves susceptible to rifampicin and isoniazid, then pyrazinamide should be ceased. Rifampicin and isoniazid are continued in the above dosage for a minimum of 6 months. If antibiotic resistance is

demonstrated on susceptibility testing, specialist consultation should be sought.
NOTE: Short course therapy is not appropriate for all patients (see below).

Short course therapy, 6 month duration (4 drugs)

This is essential if the patient has acquired their infection in an area such as S. E. Asia, where resistant organisms are common.

rifampicin 10 mg/kg/day (to a maximum daily dose of 600 mg) orally, once daily
PLUS
isoniazid 10 mg/kg/day (to a maximum daily dose of 300 mg) orally, once daily
PLUS
pyrazinamide 30 mg/kg/day (to a maximum daily dose of 2 g) orally, once daily
TOGETHER WITH EITHER
ethambutol 20 mg/kg/day (to a maximum daily dose of 1.2 g) orally, once daily for 2 months. If isoniazid resistance has been demonstrated at this time, ethambutol should be continued in a reduced dose of 15 mg/kg, once daily.
OR
streptomycin* 1 g intramuscularly, daily for patients under 40 years of age provided there is no evidence of renal impairment. A lower dose of streptomycin should be employed in older patients or in those with renal impairment. In all patients, therapy should be monitored by regular assessment of renal function and audiometric tests should be routinely used at the initiation, during, and at the cessation of streptomycin therapy.

Four drug therapy should continue for at least 2 months, by which time susceptibility results should be available. If the organism proves susceptible to rifampicin and isoniazid, then ethambutol (or streptomycin) and pyrazinamide can be ceased, and rifampicin and isoniazid continued in the above dosage for a minimum of 6 months. If antibiotic resistance is demonstrated, specialist consultation should be sought. In particular, second line drugs such as capreomycin,

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* Supplies should be available from specialist treatment centres in each State

ciprofloxacin, cycloserine or prothionamide should only be used following specialist consultation.

To be successful, short course regimens require susceptible organisms, adequate host defence mechanisms and good patient compliance. Treatment should be supervised and bacteriological conversion with negative cultures demonstrated within 2 or 3 months of treatment. If there is any doubt as to the applicability of these criteria, then short course chemotherapy is no longer appropriate, and the duration of treatment may need to be prolonged to at least 9, or even 12 to 18 months. Under these circumstances, specialist advice should be sought.

There are many other regimens of equal efficacy, including daily therapy followed by intermittently supervised twice or thrice weekly therapy. **For further information including treatment of non-pulmonary tuberculosis see: Commonwealth Department of Community Services and Health. Tuberculosis in Australia and New Zealand. 7th ed. Canberra: Australian Government Publishing Service, 1990.**

URINARY TRACT INFECTIONS

Antimicrobial therapy of urinary tract infections is assisted by a high fluid intake, complete bladder emptying, and in some instances (e.g. if aminoglycosides are used), by alkalinisation of the urine e.g. by sodium citrotartrate 4 g orally, 6-hourly.

ACUTE UNCOMPLICATED URINARY TRACT INFECTION

Any of the following regimens can usually be expected to cure 80 to 90% of uncomplicated urinary tract infections.

Treatment failures will usually be due either to a resistant organism or an unsuspected underlying abnormality of the urinary tract.

Single-dose therapy (not recommended in men, in whom underlying problems are common)

amoxycillin 3 g orally
OR
trimethoprim 600 mg orally
OR
gentamicin 120 mg intramuscularly

Multiple-dose therapy (5 day course)

amoxycillin 250 mg orally, 8-hourly
OR
trimethoprim 300 mg orally, daily
OR
cephalexin 250 mg orally, 6-hourly
OR

amoxycillin/potassium clavulanate (250/125 mg) orally, 8-hourly. This combination should not be preferred to amoxycillin alone unless resistance to amoxycillin is suspected or proven

COMPLICATED URINARY TRACT INFECTION

Attempts should be made to define or exclude any underlying anatomical or functional abnormality.

The antibiotic sensitivities of organisms cultured from complicated urinary tract infections are often difficult to predict and because therapy may need to be prolonged, high dose, and on occasions parenteral, it is most important that adequate urine cultures are performed.

Consultation with the Microbiology Department may assist in selecting the most appropriate therapeutic regimen, both for initial therapy and, if modification is required when culture and sensitivity results become available. Drugs such as amoxycillin/potassium clavulanate, cefotaxime, ceftriaxone, gentamicin and norfloxacin should be considered.

Recurrent or chronic urinary tract infections

Recurrent infections occur either as relapse of a previously treated infection or because of reinfection. In female patients, instruction on perineal hygiene, and micturition after intercourse may assist in preventing reinfection.

For the acute treatment of an episode of recurrent or chronic urinary infection (5 to 7 day course):

amoxycillin/potassium clavulanate (250/125 mg) orally, 8-hourly
OR
nitrofurantoin 50 to 100 mg orally, 6-hourly
OR
norfloxacin 400 mg orally, 12-hourly

Prophylaxis instituted after successful treatment can reduce or prevent subsequent attacks and may be continued for 3 to 6 months, or on occasions longer. Appropriate prophylactic therapy is usually given at night, but may be taken by women after intercourse.

nitrofurantoin 50 to 100 mg orally, nightly
OR

trimethoprim 150 mg orally, nightly

Suspected septicaemia

Septicaemia is more likely to occur in patients with severe underlying renal disease, urinary tract abnormalities or where there has been instrumentation of the renal tract. Treatment is designed to cover infections by organisms such as *E. coli*, Klebsiella, Enterobacter and Proteus spp., *Pseudomonas aeruginosa* and *Enterococcus faecalis*.

(amoxy)ampicillin 1 to 2 g intravenously, 6-hourly
TOGETHER WITH
gentamicin 1 to 1.5 mg/kg intravenously, 8-hourly for 7 to 10 days or until bacteriology is clarified.
Gentamicin may be replaced by cefotaxime or ceftriaxone in elderly patients or those with renal impairment (dosages as on p. 47).

The above dosage regimen will require modification in the presence of renal impairment. If infection is likely to be acquired in an environment where gentamicin-resistant organisms are endemic then an alternative protocol, using later aminogylocosides or beta-lactam antibiotics, should be planned in consultation with the Microbiology Department.

Catheter associated urinary infections

As a general rule, these should only be treated if the patient shows signs of systemic infection, eg fever, rigors or loin pain. If required, antibiotics should be selected on the basis of the most recent urine culture results. Removal of the catheter, whenever possible, makes the greatest contribution towards cure.

Prolonged or sequential courses of antibiotics given for the treatment of catheter-associated urinary tract infections, whilst the catheter remains in situ are usually unsuccessful and tend to select for organisms resistant to many antibiotics. For similar reasons, local irrigation with antibiotics should not be used.

If a catheter needs to be changed in the presence of proven urinary infection then this procedure should be preceded by a single dose of an appropriate antibiotic administered by the intramuscular or intravenous route. The choice should take into account the sensitivity of the current infecting organisms. If this information is not available, a single parenteral dose of gentamicin 2 mg/kg should be given 30 minutes before the procedure is undertaken.

SKIN, MUSCLE AND BONE INFECTIONS

IMPETIGO

May resolve with topical treatment, e.g. chlorhexidine, povidone-iodine or mupirocin. The organisms commonly encountered are *Streptococcus pyogenes, Staphylococcus aureus* or a mixture of the two. If an antibiotic is required:

(flu)cloxacillin 500 mg orally, 6-hourly for 10 days
OR
erythromycin 500 mg orally, 12-hourly for 10 days

Some strains of *Staphylococcus aureus* are resistant to erythromycin.

BOILS, CARBUNCLES AND BULLOUS IMPETIGO

The causative organism is generally *Staphylococcus aureus,* occasionally in association with *Streptococcus pyogenes.*

If the lesions are small or few in number they may be managed by local antiseptics and drainage. If lesions are extensive or cause systemic symptoms an antibiotic is required:

(flu)cloxacillin 500 mg orally, 6-hourly
OR
erythromycin 500 mg orally, 12-hourly

Some strains of *Staphylococcus aureus* are resistant to erythromycin.

CELLULITIS AND ERYSIPELAS

Streptococcus pyogenes is classically the causative organism

Severe

benzylpenicillin 1.2 g intravenously, 4-hourly

Less severe

procaine penicillin 1 g intramuscularly 12-hourly
OR
phenoxymethylpenicillin 500 mg orally, 6-hourly

In a patient who is hypersensitive to penicillin, cephalothin or vancomycin may be used (*Staphylococcus aureus*).

Staphylococcus aureus - if suspected

Severe and possibly life-threatening

(flu)cloxacillin 2 g intravenously, 4 to 6-hourly

In a patient who is hypersensitive to penicillin, cephalothin 2 g intravenously, 4 to 6-hourly may be substituted for the above regimen. If there is a history of SEVERE penicillin hypersensitivity vancomycin 1 g intravenously, 12-hourly should be used, each dose to be infused over not less than 1 hour.

Less severe

(flu)cloxacillin 500 mg to 1 g orally, 6-hourly
OR
cephalexin 500 mg orally, 6-hourly
OR
erythromycin 500 mg orally, 12-hourly

SUPPURATIVE WOUND INFECTIONS (SURGICAL OR TRAUMATIC)

Local measures such as surgical drainage, irrigation with isotonic stabilised sodium hypochlorite solution*, saline dressings or use of a local antiseptic such as povidone-iodine usually suffice. Topical use

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* Health Department Victoria. "Staphylococcal Infections in Hospitals", 3rd Ed., 1987, p. 22.

of antibiotics may cause the emergence of resistant organisms and is not recommended.

If there is surrounding cellulitis and/or systemic symptoms are present, treat as above for staphylococcal cellulitis. If Gram-negative organisms are suspected or known to be involved, use cephalexin orally or cephalothin intravenously or gentamicin 1 to 1.5 mg/kg intravenously or intramuscularly, 8-hourly.

VARICOSE OR DECUBITUS ULCERS

Local measures including those for suppurative wound infections are most important. If there is surrounding cellulitis, treat with systemic antibiotics (see p. 29). Where there is extensive tissue damage, anaerobic organisms are likely to be involved and

metronidazole 400 mg orally, 12-hourly should be added

BITES

Both animal and human bites commonly become infected with mouth flora. In animal bites *Pasteurella multocida* is commonly involved. Adequate wound toilet is important but even if overt infection is not present all bites should be treated with

phenoxymethylpenicillin 500 mg orally, 6-hourly for 5 days
OR
procaine penicillin 1 g intramuscularly, daily, for 5 to 7 days

If severe infection is present or response to the above regimens is poor, parenteral treatment with other antibiotics or surgical drainage may be needed

CLOSTRIDIAL INFECTION

The basis of treatment of clostridial infection is surgical debridement and antibiotic therapy. Hyperbaric oxygen is an important adjunct if available.

Cellulitis

benzylpenicillin 1.2 g intravenously, 4-hourly

Myositis (gas gangrene)

benzylpenicillin 2.4 g intravenously, 4-hourly
If the patient is allergic to penicillin, use metronidazole 500 mg intravenously, 8-hourly (infused over 20 minutes). Other measures are vitally important and require expert advice.

SYNERGISTIC GANGRENE OR NECROTISING FASCIITIS

The basis of treatment of synergistic gangrene is operative removal of devitalised tissue. Neither antibiotics nor hyperbaric oxygen are substitutes for surgical debridement. Causative organisms are usually mixed aerobes and anaerobes, e.g. *E. coli, Bacteroides fragilis,* streptococci and staphylococci.

benzylpenicillin 1.2 to 2.4 g intravenously, 4-hourly
PLUS
gentamicin 1 to 1.5 mg/kg intravenously or intramuscularly, 8-hourly
PLUS
metronidazole 500 mg intravenously, 8-hourly, (infused over 20 minutes), or 1 g rectally, 8-hourly depending upon the clinical condition of the patient

For patients who are hypersensitive to penicillin

clindamycin 600 mg intravenously, 8-hourly (dilute in 100 ml, infuse over at least 30 minutes)
PLUS
gentamicin 1 to 1.5 mg/kg intravenously or intramuscularly, 8-hourly

Depending on the organisms subsequently isolated, other antibiotic combinations may be indicated e.g. (flu)cloxacillin if *Staphylococcus aureus* is present.

DIABETIC FOOT INFECTIONS

These should always be regarded as serious and should be treated vigorously. Anaerobic organisms are almost always involved, often with mixed Gram-positive and Gram-negative aerobic organisms. Surgical debridement is often necessary and antibiotic treatment should be effective against the mixed aerobic and anaerobic

organisms frequently responsible. Underlying osteomyelitis should be considered.

metronidazole 400 to 500 mg orally, 12-hourly
PLUS
cephalexin 500 mg orally, 6-hourly
OR (AS A SINGLE AGENT)
amoxycillin/potassium clavulanate (500/125 mg) orally, 8-hourly

In severe infections

metronidazole 500 mg intravenously, 12-hourly (each dose infused over 20 minutes) or 1 g suppository rectally, 12-hourly
PLUS
cephalothin 1 g intravenously, 6-hourly

The duration of treatment will depend upon the response.

COMPOUND FRACTURES

Prophylaxis or early treatment directed particularly against *Staphylococcus aureus* and *Clostridium perfringens* should be given.

(flu)cloxacillin 1 g intravenously, 4 to 6-hourly

If wound soiling or tissue damage is severe, gentamicin 1.5 mg/kg intravenously, 8-hourly may be added.

The patient's immune status to tetanus should be reviewed.

Duration of treatment will vary, but 1 to 3 days is appropriate unless infection is clearly established or there was prolonged contamination of the wound before commencement of therapy.

OSTEOMYELITIS / SEPTIC ARTHRITIS

It is important to obtain suitable specimens for culture. Note that in chronic infections, sinus cultures may be misleading. Sequestra, dead bone or foreign material require surgical removal in chronic infection, or in acute infection which fails to resolve.

In adults, treat as *Staphylococcus aureus* infection unless another causative organism is identified.

(flu)cloxacillin 2 g intravenously, 4 to 6-hourly for 3 to 4 weeks (acute osteomyelitis), 2 to 4 weeks (acute septic arthritis) or 2 to 6 weeks (chronic bone or joint infection)
FOLLOWED BY

(flu)cloxacillin 1 g orally, 6-hourly until total duration of treatment is 4 to 6 weeks (acute infection) or many months (chronic infection). If acute infection is complicated by the presence of foreign material (e.g. joint prostheses, metal rods, plates or screws), treatment should be continued for at least 3 months.

In children under 5 years of age with septic arthritis, (amoxy)-ampicillin, cefotaxime or ceftriaxone should be added to the initial (flu)cloxacillin treatment in age-related dosages, as *Haemophilus influenzae* is a common cause of septic arthritis in this age group. If no organism is isolated, treatment should be continued with (flu)cloxacillin orally together with (amoxy)ampicillin orally, or with amoxycillin/potassium clavulanate orally alone.

When (flu)cloxacillin is administered orally, it is necessary to achieve adequate serum levels, which should be checked. The addition of probenecid 500 mg orally, 6-hourly, may be necessary to achieve adequate serum levels. If the (flu)cloxacillin results in nausea and/or vomiting, the dose may be reduced to 500 mg orally, 6-hourly with probenecid, provided that adequate serum levels are attained.

If the patient is hypersensitive to penicillin, cephalothin 2 g intravenously, 4-hourly should be substituted for intravenous (flu)cloxacillin, followed by cephalexin 1 g orally, 6-hourly. If there is a history of SEVERE penicillin hypersensitivity, clindamycin 600 mg intravenously, 8-hourly should be used (each dose to be diluted in 100 ml and infused over at least 30 minutes), followed by 300 mg orally, 8-hourly.

In chronic infections, supervised therapy is required for many months and should be carried out in consultation with a clinical microbiologist or infectious disease physician.

If infection is shown to be caused by a Gram-negative bacillus, treatment is more difficult, particularly in the presence of foreign material, and should be carried out in consultation with a clinical microbiologist or infectious disease physician.

ALIMENTARY TRACT INFECTIONS

ORAL AND DENTAL INFECTIONS

Causative organisms are usually mixed anaerobic and aerobic oral flora. In virtually all instances, referral to a dental surgeon is advisable to exclude or treat any underlying cause.

Gingival infections

In the absence of systemic signs or symptoms, antibiotic therapy is not usually indicated and local dental care to control bacterial plaque will often suffice. If accompanied by systemic signs or symptoms:

procaine penicillin 1 g intramuscularly, daily for 5 days
OR
phenoxymethylpenicillin 500 mg orally, 6-hourly for 5 days
OR
metronidazole 200 to 250 mg orally, 8-hourly for 5 days

and refer for dental management.

In severe cases both procaine penicillin and metronidazole may be required.

Pericoronitis or tooth abscess

In the absence of systemic signs or symptoms, antibiotic therapy is not usually indicated and local dental care will often suffice. In pericoronitis, vigorous warm mouth rinses with saline or 1:200 chlorhexidine and a topical paint e.g. povidone-iodine, helps greatly. In the case of a tooth abscess, removal of the infected pulp tissue, with or without drainage, is usually required. If accompanied by systemic signs or symptoms:

procaine penicillin 1 g intramuscularly, daily for 3 days
OR (for the milder case)

phenoxymethylpenicillin 500 mg orally, 6-hourly for 2 to 3 days
OR (if unresponsive)
amoxycillin/potassium clavulanate (250/125 mg) orally, 8-hourly
OR (if hypersensitive to penicillin)
clindamycin 300 mg intravenously, 8-hourly or 300 mg orally, 8-hourly for 2 to 3 days

Oral candidiasis

Local cleaning care, especially beneath dentures, is of assistance.

amphotericin 1 lozenge (10 mg) dissolved slowly in the mouth, 6-hourly for 7 to 14 days
OR
nystatin 1 lozenge (100,000 units) dissolved slowly in the mouth, 6-hourly for 7 to 14 days.
Nystatin suspension may be used if the lozenge cannot be tolerated e.g. in infants.

In HIV infections, these agents are usually not sufficient and ketoconazole may be considered using a dosage of 200 mg orally, daily.

ACUTE CHOLECYSTITIS

Causative organisms are usually aerobic bowel flora, e.g. *E. coli,* Klebsiella spp. and less commonly *Enterococcus faecalis.* When antimicrobial therapy is indicated on clinical grounds, the following are recommended:

(amoxy)ampicillin 1 g intravenously, or intramuscularly, 4 to 6-hourly
USUALLY TOGETHER WITH
gentamicin 1.5 mg/kg intravenously, or intramuscularly, 8-hourly
OR (AS A SINGLE AGENT)
a cephalosporin intravenously or intramuscularly either cephalothin 1 g intravenously, 4 to 6-hourly, or cephazolin 500 mg to 1 g intramuscularly, 8-hourly, or cephamandole 1 g intravenously, 8-hourly for 5 to 10 days

Ascending cholangitis is usually associated with septicaemia. See suggested treatment regimen on p. 47.

ACUTE PERITONITIS

This is usually a polymicrobic infection caused by aerobic and anaerobic bowel flora. The aerobic bowel flora are most likely to produce mortality due to septicaemia while the anaerobes commonly cause morbidity due to intra-abdominal abscesses and wound infection. Elimination of only a proportion of this flora may be associated with a satisfactory outcome if the patient's host defences can cope with what remains. Thus, for a mild case a single broad-spectrum antibiotic may suffice, whereas for a severe case a multiple drug regimen provides the best cover, albeit at a greater risk of toxicity.

Multiple drug regimens

(amoxy)ampicillin 2 g intravenously, 6-hourly
TOGETHER WITH
gentamicin 1.5 mg/kg intravenously, 8-hourly
TOGETHER WITH EITHER
metronidazole 500 mg intravenously, 8-hourly, (each dose infused over 20 minutes). Metronidazole suppositories (1 g, 8-hourly) may be substituted for the intravenous form, depending upon the condition of the patient
OR
clindamycin 600 mg intravenously, 8-hourly (each dose to be diluted in 100 ml and infused over at least 30 minutes)

For the patient hypersensitive to penicillin, (amoxy)ampicillin may be omitted but this combination will not cover *Enterococcus faecalis*.

Single drug regimens

cefoxitin 2 g intravenously, 8-hourly

The results with this regimen in general have been good, although it does not cover *Enterococcus faecalis*, some Bacteroides species nor a small proportion of aerobic Gram-negative bowel flora. For these reasons some clinicians do not recommend cefoxitin alone for generalised peritonitis.
OR
ticarcillin/potassium clavulanate 3/0.1 g intravenously, 4 to 6-hourly
OR

imipenem/cilastatin 1 g intravenously, 6-hourly

The above two regimens have good activity against both Gram-negative aeroboc and anaerobic bacilli. However, imipenem/cilastatin is at present very expensive.

The newer third generation cephalosporins, cefotaxime and ceftriaxone, have a wider spectrum of activity than cefoxitin against aerobic enteric bacilli, but they are not ideal as single drugs for the treatment of peritonitis, because their anaerobic cover may be inadequate. Both would be suitable for such therapy if combined with metronidazole.

ACUTE PANCREATITIS

Antibiotics are not usually indicated in the acute management of this disease. If bacterial infection is thought to have supervened, the treatment is as for acute peritonitis.

ANTIBIOTIC-ASSOCIATED DIARRHOEA

The first step is to cease treatment with any antibiotic likely to be causing the symptoms. Sigmoidoscopy or colonoscopy may assist in assessing severity. A proportion of cases is due to toxigenic *Clostridium difficile* and such cases, when proven or suspected, should be treated as follows:

If mild or moderate

metronidazole 200 to 500 mg orally, 8-hourly for 7 to 14 days
OR
bacitracin 25,000 units (capsules) orally, 6-hourly for 7 to 14 days. (This preparation is not commercially available but may be prepared by hospital pharmacy departments).

If severe or relapsing

vancomycin 125 mg orally, 6-hourly for 7 to 14 days

ACUTE ENTERIC INFECTIONS

Typhoid/Paratyphoid fever

chloramphenicol 500 to 750 mg orally, 6-hourly for 14 days
OR
co-trimoxazole (double strength i.e. 160/800 mg) 1 tablet orally, 12-hourly for 14 days
OR
amoxycillin 1 g orally, 6-hourly for 14 days
In order to minimise relapse, some clinicians supplement the above regimens with a further 14 days of amoxycillin or co-trimoxazole. In severe cases the drugs should be given intravenously in the same dosage for the first 4 to 5 days of treatment.

If strains resistant to the above three antimicrobials are suspected or proven:

ciprofloxacin 500 mg orally, 12-hourly for 14 days

The long-term asymptomatic carrier state is a difficult problem and expert advice should be sought.

Diarrhoeal Disease

There are many bacterial causes of diarrhoea such as enterotoxigenic *E.coli Campylobacter jejuni,* Salmonella and Shigella species. In general, antibiotic therapy is not recommended in uncomplicated diarrhoeal diseases except in the following situations:

Cholera

Antibiotic therapy reduces the volume and duration of diarrhoea.

doxycycline 100 mg orally, 12-hourly for 4 days
OR
co-trimoxazole (double strength, ie. 160/800 mg) 1 tablet orally 12-hourly for 4 days

Shigellosis

Mild shigellosis does not require antibiotic therapy. However, in moderate and severe dysentery, antibiotic treatment is indicated. The pattern of antibiotic susceptibility of Shigella strains varies from country to country, and many resistant strains are encountered. Depending on the country in which the organism was acquired antibiotic therapy may have to be modified according to the results of culture and sensitivity tests.

Regimens include:

ampicillin 100 mg/kg/day orally, in 4 divided doses for 7 to 10 days (amoxycillin is probably less effective than ampicillin)
OR
co-trimoxazole (double strength, i.e 160/800 mg) 1 tablet orally, 12-hourly for 7 to 10 days
OR
norfloxacin 400 mg orally, 12-hourly for 7 to 10 days

Salmonella enteritis

Antibiotic treatment is not generally advisable as it is not clinically beneficial and it may prolong excretion of pathogenic organisms. Antibiotics are not indicated for the asymptomatic short-term carrier state. However, antibiotic therapy is necessary for bacteraemia or systemic involvement which are more likely to occur in babies, malnourished children and immunosuppressed or elderly people. The choice of drugs and their dosages are the same as in the treatment of typhoid fever. For certain patients in whom eradication of Salmonella organisms is important e.g. those with AIDS, other immunosuppressed patients such as those with renal transplants, food handlers and possibly elderly and debilitated patients, ciprofloxacin 500 to 750 mg orally, 12-hourly for 5 to 7 days may be considered.

Eradication should not be presumed without performing stool cultures. Specialist advice should be sought.

Campylobacter enteritis

Chemotherapy is unnecessary in most cases. Erythromycin 500 mg orally, 6-hourly for 7 to 10 days may be justified in severe cases and also in patients in special circumstances (e.g. food handlers) as this therapy may shorten the carrier state which follows the resolution of symptoms.

Acute giardiasis

tinidazole 2 g orally, as a single dose
OR
metronidazole 200 to 500 mg orally, 8-hourly for 7 days
OR
benzoyl metronidazole suspension 20 to 30 mg/kg/day orally, in 3 divided doses for 7 days

Acute intestinal amoebiasis

metronidazole 600 to 800 mg orally, 8-hourly for 6 to 10 days
FOLLOWED BY
diloxanide furoate 500 mg orally, 8-hourly for 10 days
Specialist advice should be sought.

CARDIOVASCULAR SYSTEM INFECTIONS

ENDOCARDITIS

There are two important principles:

- Initial treatment must be given INTRAVENOUSLY.
- Duration of therapy should usually be FOUR TO SIX WEEKS.

There are several alternative regimens reported in the literature and consultation with an infectious disease physician or clinical microbiologist should be sought. Surgical consultation should be considered. The use of an aminoglycoside in combination with a penicillin adds to the risk of toxicity, but for certain pathogens (see below), this practice improves the chance of a favourable outcome. Minimal inhibitory concentration (MIC) and, in particular, minimal bactericidal concentration (MBC) determinations may be helpful in choosing the optimal regimen and synergy studies may further assist. The patient's response to therapy should be monitored clinically and by laboratory studies, where appropriate. Serum gentamicin or vancomycin levels should be monitored closely. Follow-up blood cultures and serum bacteriostatic and bactericidal levels may be useful in patients responding poorly.

Empirical therapy

The prompt empirical use of antimicrobials before a pathogen is isolated is necessary in patients with fulminating infection suspected to be due to endocarditis. However, even in these patients three sets of blood cultures and other appropriate microbiological specimens must be obtained before therapy is commenced

benzylpenicillin 1.2 g intravenously, 4-hourly
TOGETHER WITH

(flu)cloxacillin 2 g intravenously, 4-hourly
TOGETHER WITH
gentamicin 1.5 mg/kg intravenously, 8-hourly
OR in special circumstances e.g. in hospital-acquired infection or patients hypersensitive to penicillin
vancomycin 1 g intravenously, 12-hourly or 500 mg intravenously, 6-hourly, each dose to be infused over at least 1 hour
TOGETHER WITH
gentamicin 1.5 mg/kg intravenously, 8-hourly

This regimen should be modified as soon as the organism and its sensitivity pattern are known. Most cases of fulminating endocarditis are caused by *Staphylococcus aureus*.

Endocarditis caused by specific bacteria

Streptococcal or enterococcal endocarditis

Most streptococci causing endocarditis are highly sensitive to benzylpenicillin and will usually be identified as members of the viridans group of Streptococci.

Streptococci highly sensitive to benzylpenicillin

Most of these have both MIC and MBC less than 0.2 mg/L but a few show tolerance, i.e. have an MBC/MIC ratio >4. The most reliable regimen (which should always be used for infection involving a tolerant strain) is

benzylpenicillin 1.2 to 1.8 g, intravenously, 4-hourly for 4 weeks
TOGETHER WITH
gentamicin 1 mg/kg intravenously, 8-hourly for 2 weeks

Shorter or simplified regimens for highly sensitive non-tolerant organisms are:

benzylpenicillin 1.2 to 1.8 g intravenously, 4-hourly for 4 weeks (as a single agent)
OR
benzylpenicillin 1.2 to 1.8 g intravenously, 4-hourly for 2 weeks
TOGETHER WITH
gentamicin 1 mg/kg intravenously, 8-hourly for 2 weeks

After 2 weeks of intravenous therapy, replacement with oral penicillin may occasionally be considered but only when monitoring

of antibiotic levels can be undertaken. An acceptable regimen is phenoxymethylpenicillin 500 mg orally, 6-hourly with probenecid 500 mg orally, 6-hourly.

Enterococci and streptococci relatively resistant to benzylpenicillin, (both MIC & MBC > 0.2 mg/L)

benzylpenicillin 1.2 to 1.8 g intravenously, 4-hourly for 6 weeks
TOGETHER WITH
gentamicin 1 mg/kg intravenously, 8-hourly for six weeks

This is one of the few indications for prolongation of gentamicin therapy beyond 2 weeks. Although a relatively low dose of gentamicin is used in this regimen, serum levels should be monitored regularly.
NOTE: Some physicians prefer to use (amoxy)ampicillin (2 g every 4 hours) together with gentamicin, instead of the above for enterococcal endocarditis. The therapeutic efficacy is similar.

Staphylococcal endocarditis

Staphylococci sensitive to methicillin and (flu)cloxacillin

(flu)cloxacillin 2 g intravenously, 4-hourly for 6 weeks
TOGETHER WITH
gentamicin 1 mg/kg intravenously, 8-hourly for 1 or 2 weeks

Because of the need for surgical intervention in a significant number of patients, early consultation with a cardiovascular surgeon is recommended

Staphylococci resistant to methicillin (including MRSA) and hence all beta-lactam antibiotics*

vancomycin 1 g intravenously, 12-hourly or 500 mg intravenously, 6-hourly for 6 weeks, each dose to be infused over not less than 1 hour. Serum levels should be monitored regularly.

Gram-negative bacterial endocarditis

This is uncommon, but such patients frequently require cardiac surgery in combination with antimicrobial therapy. Early consultation

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* MRSA commonly appear sensitive to cephalosporins in laboratory testing but do not respond to these drugs *in vivo*.

with a cardiovascular surgeon, and clinical microbiologist or infectious disease physician is recommended.

"Culture-negative" endocarditis

This may be due to prior antibiotic therapy or unusual micro-organisms such as fastidious streptococci, *Coxiella burnetii* (the cause of Q fever) and fungi, including *Candida albicans*. Unless Q fever or fungal infection is strongly suspected, patients with culture negative endocarditis should be commenced empirically on benzylpenicillin plus gentamicin, as for enterococcal endocarditis (see p. 42).

Prosthetic valve endocarditis

Potential pathogens include staphylococci, particularly *Staphylococcus epidermidis*, Corynebacterium spp, Streptococcus spp, Enterobacteriaceae, *Pseudomonas aeruginosa, Candida albicans* and other fungi. Because of increasing resistance of *Staphylococcus epidermidis* to flucloxacillin, initial empirical therapy should include vancomycin, plus gentamicin in most hospitals. Early consultation with a cardiovascular surgeon and an infectious disease physician or clinical microbiologist is recommended.

An initial regimen which is broad-spectrum, bactericidal but with additive toxicity could be:

vancomycin 1 g intravenously, 12-hourly or 500 mg intravenously, 6-hourly, each dose to be infused over at least 1 hour

TOGETHER WITH

gentamicin 1.5 mg/kg intravenously, 8-hourly

Endocarditis in patients hypersensitive to penicillin

In these patients, consultation with an infectious disease physician or clinical microbiologist should be sought.

Initial empirical therapy could be

> vancomycin 1 g intravenously, 12-hourly, each dose to be infused over not less than 1 hour. (This does not cover the uncommon possibility of a Gram-negative bacterial endocarditis.)

Because of potential toxicity, serum concentrations of vancomycin should be monitored.

In staphylococcal or streptococcal (not enterococcal) endocarditis, cephalothin can usually be substituted for vancomycin, unless the previous reaction to penicillin was severe.

SEPTICAEMIA

Patients with clinical features of septicaemia require urgent empirical therapy. This should be instituted immediately after microbiological specimens, including blood cultures (three sets preferred) have been obtained. The treatment regimens are set out as follows

Part A Recommended "best guess" initial therapy based on the predicted source of an infection and the usual susceptibility of common pathogens.

Part B Empirical therapy where there is no obvious source of infection, with regimens provided for both normal and immunosuppressed patients.

Part C Directed therapy for infection due to specific organisms when microbiological results are available.

A. RECOMMENDED INITIAL REGIMENS FOR INFECTION PRESUMED TO HAVE ARISEN FROM:

Urinary tract

Septicaemia is usually due to the Enterobacteriaceae or *Enterococcus faecalis* but, in complicated urinary tract infections, staphylococci and *Pseudomonas aeruginosa* are occasional pathogens.

(amoxy)ampicillin 1 to 2 g intravenously, 6-hourly
TOGETHER WITH
gentamicin 1.5 mg/kg intravenously, 8-hourly

In a patient who is hypersensitive to penicillin, a cephalosporin (e.g. cephalothin 1 to 2 g intravenously, 4 to 6-hourly) may be substituted for (amoxy)ampicillin in the above regimen with due caution and bearing in mind that 3% to 6% of patients with penicillin hypersensitivity will also react to cephalosporins.

Alternatively:

cefotaxime 1 to 2 g intravenously, 8-hourly
OR
ceftriaxone 1 to 2 g intravenously, 24-hourly may be given alone but these regimens do not provide adequate cover for *Pseudomonas aeruginosa.*

Biliary or gastrointestinal tract including ascending cholangitis

Likely pathogens include Enterobacteriaceae, anaerobes, particularly anaerobic cocci and *Bacteroides fragilis,* and less often, *Enterococcus faecalis.*

* gentamicin 1.5 mg/kg intravenously, 8-hourly
PLUS
metronidazole 500 mg intravenously, 12-hourly (each dose to be infused over 20 minutes)
TOGETHER WITH EITHER
(amoxy) ampicillin 1 to 2 g intravenously, 4-hourly
OR
benzylpenicillin 1.2 g intravenously, 4-hourly

Female genital tract

Usual pathogens include anaerobic bacteria, particularly anaerobic cocci, Enterobacteriaceae, streptococci, and occasionally, staphylococci.

(amoxy)ampicillin 1 g intravenously, 4-hourly
TOGETHER WITH
* gentamicin 1.5 mg/kg intravenously, 8-hourly
TOGETHER WITH

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* If the use of an aminoglycoside is undesirable, cefotaxime 1 to 2 g intravenously, 8-hourly may be substituted for gentamicin. Alternatively, a ureidopenicillin may be used as a single agent for the treatment of ascending cholangitis.

In the penicillin hypersensitive patient, cephalothin 2 g intravenously, 6-hourly may be substituted for (amoxy)ampicillin or benzylpenicillin, bearing in mind that 3% to 6% of patients with penicillin hypersensitivity will also cross-react to cephalosporins.

metronidazole 500 mg intravenously, 12-hourly (each dose to be infused over 20 minutes)

Alternative therapy may include substituting clindamycin 600 mg intravenously, 8-hourly (dilute in 100 ml and infuse over at least 30 minutes) or a second generation cephalosporin eg. cefoxitin 2 g intravenously, 6-hourly for the two drug combination of (amoxy)ampicillin and metronidazole in the above regimen. These alternative combinations will not cover *Enterococcus faecalis*.

Skin

Carbuncle

Staphylococcus aureus is the most likely pathogen.

(flu)cloxacillin 1 to 2 g intravenously, 4-hourly

Cellulitis

Streptococcus pyogenes is the most likely pathogen but *Staphylococcus aureus* may occur occasionally.

benzylpenicillin 1.2 g intravenously, 4-hourly
TOGETHER WITH
(flu)cloxacillin 1 to 2 g intravenously, 4-hourly until diagnosis is clarified.

Once a microbiological diagnosis is made, the less appropriate antibiotic should be ceased.

For the patient who is hypersensitive to penicillin, cephalothin 2 g intravenously, 4 to 6-hourly may be substituted for (flu)cloxacillin and benzylpenicillin bearing in mind that 3% to 6% of patients with penicillin hypersensitivity will also cross-react to cephalosporins.

Decubitus and ischaemic ulcers, diabetic foot infections

Pathogens may include *Staphylococcus aureus*, Enterobacteriaceae and anaerobes.

(flu)cloxacillin 1 g intravenously, 4-hourly
TOGETHER WITH

gentamicin 1.5 mg/kg intravenously, 8-hourly
TOGETHER WITH
metronidazole 500 mg intravenously, 12-hourly (infused over 20 minutes)

Alternative therapy with a single preparation would be ticarcillin/potassium clavulanate 3/0.1 g intravenously, 4-hourly.

Intravascular cannulae, including central venous lines

Prior to commencement of therapy the cannula should be removed, peripheral blood cultures taken and the catheter tip also submitted for culture. *Staphylococcus aureus* and *Staphylococcus epidermidis* are the most likely pathogens followed by Candida spp and Enterobacteriaceae.

(flu)cloxacillin 1 to 2 g intravenously, 4-hourly
TOGETHER WITH
gentamicin 1.5 mg/kg intravenously, 8-hourly

If septicaemia is suspected but the patient is not seriously ill it may be appropriate to obtain specimens for culture, remove the cannula and observe the patient for 12 to 24 hours, before deciding whether antimicrobial therapy is indicated.

NOTE: In patients who are hypersensitive to penicillin, (or immunocompromised patients in whom multi-resistant Gram-positive organisms are most likely), vancomycin 1 g intravenously, 12-hourly, each dose to be infused over not less than 1 hour, may be substituted for (flu)cloxacillin. Similarly in hospital units where methicillin-resistant staphylococci are prevalent, vancomycin may again be substituted until culture and sensitivity results are available.

Lung

Normal host, community-acquired lobar pneumonia

Streptococcus pneumoniae is the most likely pathogen.

benzylpenicillin 0.6 to 1.2 g intravenously, 4-hourly

Pneumonia acquired in hospital or associated with concurrent medical illness, e.g. alcoholism, malnutrition

The most common pathogens include Enterobacteriaceae, *Streptococcus pneumoniae*, other streptococci and anaerobic mouth flora. *Staphylococcus aureus* is an occasional cause.

benzylpenicillin 0.6 to 1.2 g intravenously, 4-hourly
TOGETHER WITH
gentamicin 1.5 mg/kg intravenously, 8-hourly
OR (AS A SINGLE AGENT) a later cephalosporin such as cefotaxime 1 to 2 g intravenously, 8-hourly, or ceftriaxone 1 to 2 g intravenously, 24-hourly.

Aspiration pneumonitis proven or suspected (e.g. comatose patients)

metronidazole 500 mg intravenously, 12-hourly, may be added to benzylpenicillin if community-acquired, or to benzylpenicillin plus gentamicin or a cephalosporin, if hospital-acquired.

B. EMPIRICAL THERAPY, NO SOURCE OF INFECTION OBVIOUS

Normal host

(flu)cloxacillin 2 g intravenously, 4-hourly
TOGETHER WITH
gentamicin 1.5 mg/kg intravenously, 8-hourly

Immunosuppressed patient

The most likely pathogens include Enterobacteriaceae, *Pseudomonas aeruginosa* and staphylococci. The initial therapy of febrile episodes in these patients will usually require a combination of an aminoglycoside (gentamicin or tobramycin) with a broad spectrum beta-lactam such as ticarcillin, or a third generation cephalosporin. If antibiotic-resistant organisms are prevalent in a particular unit or institution, consultation regarding a different antibiotic regimen, using reserve antibiotics, is recommended e.g. if more than 5% of local isolates show resistance to gentamicin then, with specialist advice, amikacin may need to be substituted for gentamicin.

These recommendations may not be appropriate for patients with acquired immune deficiency syndrome (AIDS).

INFECTIONS DUE TO SPECIFIC ORGANISMS

Pseudomonas aeruginosa

gentamicin (or tobramycin) 1.5 mg/kg, intravenously, 8-hourly
TOGETHER WITH
ticarcillin 3 g intravenously, 4-hourly (or an equivalent antipseudomonal penicillin)

The duration of therapy varies from 2 to 6 weeks, depending on the primary site of infection.

Methicillin-resistant *Staphylococcus aureus*

vancomycin 1 g intravenously, 12-hourly, each dose to be infused over not less than 1 hour

The average duration of therapy may be as short as 1 to 2 weeks for sepsis associated with intravenous lines provided these have been removed promptly. For deep-seated infections, such as endocarditis therapy should be continued for up to 6 weeks. Drug levels should be monitored.

An alternative regimen suitable for continuation of therapy following intravenous vancomycin is

rifampicin 600 mg orally, per day
TOGETHER WITH
fusidic acid 500 mg orally, 8-hourly

CENTRAL NERVOUS SYSTEM INFECTIONS

MENINGITIS

The three common causes of bacterial meningitis (except in neonates) are *Haemophilus influenzae* type b, *Neisseria meningitidis* and *Streptococcus pneumoniae;* the first is rare in adults.

Causative organism not yet known

CSF Gram stain or rapid antigen testing may enable an immediate aetiological diagnosis, but since all three common pathogens are usually susceptible to chloramphenicol or a third generation cephalosporin, either may be used alone as empirical therapy. The dosage is as recommended for *H. influenzae* type b meningitis. It is acceptable to give benzylpenicillin (dosage as for meningococcal meningitis) as well, and discontinue the less appropriate drug when an organism is isolated. For children, in areas where chloramphenicol resistant strains of *H. influenzae* are found, a third generation cephalosporin (such as cefotaxime or ceftriaxone) should be used alone for initial therapy (but will not cover *Listeria*). Dosage is as recommended for *H. influenzae* type b meningitis.

Causative organism known

Regimens for the three common forms of meningitis are:

Haemophilus influenzae type b

a third generation cephalosporin e.g.

cefotaxime 200 mg/kg/day intravenously, in 4 divided doses 6-hourly, in children. In adults, 1 g intravenously, 6-hourly

OR

ceftriaxone 100 mg/kg/day intravenously, in 1 to 2 divided doses, in children. In adults, 2 g/day intravenously in 1 to 2 divided doses

OR

chloramphenicol 80 to 100 mg/kg/24 hours, intravenously* in 4 divided doses, in children. In adults, 750 mg to 1 g intravenously, 6-hourly.

In 3 to 4 days, when the patient is well enough to take oral medication, chloramphenicol can be given orally#, in the same dosage.

The total duration of treatment should be 10 to 14 days.

(Amoxy)ampicillin is not now recommended for empirical treatment because of the increasing incidence of (amoxy)ampicillin-resistant strains of *H. influenzae*.

Contacts: *H. influenzae* type b may spread to close contacts, particularly children. Advice should be sought from the State Health Authority, a clinical microbiologist or infectious disease physician about the need to give such contacts and the index case a 4 day course of rifampicin to prevent secondary cases (600 mg orally, twice daily in adults, 10 mg/kg orally, twice daily in children).

Meningococcal

benzylpenicillin 1.2 to 1.8 g intravenously, 4-hourly for 5 to 7 days

Like Haemophilus, the meningococcus may also spread to close contacts. A 2 day course of rifampicin should be given to such contacts and the index case to prevent secondary cases (600 mg orally, twice daily in adults, 10 mg/kg orally, twice daily for children). Alternatively, where compliance is a problem, a single intramuscular dose of ceftriaxone (5 mg/kg to a maximum of 250 mg) may be appropriate.

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* Assay of serum chloramphenicol levels should be considered in high dosage treatment regimens to avoid dose-related toxicity.

The paediatric suspension of chloramphenicol palmitate may be inadequately absorbed in some children; assay of serum chloramphenicol levels may be indicated to ensure adequate therapy.

Pneumococcal

benzylpenicillin 1.2 to 1.8 g intravenously, 4-hourly for 10 to 14 days

A few very ill patients may require treatment for up to 21 days.

Special Considerations

Intrathecal therapy is not recommended but intra-ventricular treatment may sometimes be valuable, for example in Gram-negative and fungal meningitis. Earlier cephalosporins and systemic aminoglycosides are not effective in the treatment of meningitis. However, newer cephalosporins, such as cefotaxime, ceftriaxone and ceftazidime have proved useful in treating enteric Gram-negative bacillary meningitis.

Consultation with either a clinical microbiologist or infectious disease physician experienced in this field should be sought if there is any uncertainty in treating a patient with meningitis. Consultation is particularly advisable in the case of:

1. Patients who are hypersensitive to penicillin.
2. Meningitis complicating surgery (particularly shunts).
3. Enteric Gram-negative bacterial meningitis (particularly Pseudomonas infections).
4. Neonatal meningitis.
5. Unusual organisms, e.g. *Cryptococcus* (see below), *Listeria*.
6. Unusually resistant organisms eg. penicillin-resistant pneumococci or chloramphenicol-resistant *H. influenzae*.
7. Poor clinical response.

Cryptococcal meningitis

A suggested regimen is:

amphotericin 0.5 mg/kg/day intravenously, by slow infusion over 6 hours (following a test dose of 1 mg and daily increments of 5 to 10 mg) for 6 weeks. In severe or life-threatening infections where it may be required to reach therapeutic blood levels more rapidly, a test dose of 5 mg administered over 1 hour, followed by the balance of the daily dose over the next 6 hours, may be used. This may require the use of antihistamines and/or corticosteroids before each dose

TOGETHER WITH (for sensitive organisms)

flucytosine approximately 150 mg/kg/day, orally or intravenously, in 4 divided doses for 6 weeks. This is contraindicated in bone marrow depression. Blood levels of flucytosine should be monitored because renal impairment often occurs in amphotericin toxicity.

HERPES SIMPLEX ENCEPHALITIS (suspected or proven)

acyclovir 10 mg/kg intravenously, 8-hourly for 10 to 14 days, each dose to be infused over not less than 1 hour.

BRAIN ABSCESS

The infecting organism(s) vary with the underlying predisposing cause, but most brain abscesses are polymicrobic with microaerophilic cocci, including *Streptococcus milleri*, and anaerobic bacteria predominating. However, where the likely site of origin is the ear or paranasal sinuses, enteric Gram-negative bacilli are commonly involved, while after trauma or surgery *Staphylococcus aureus* must be considered. Appropriate antimicrobial treatment is essential and should be complemented by surgical drainage where possible.

Consultation with either a clinical microbiologist or infectious disease physician in addition to surgical assessment is advised.

The following alternatives are suggested, but may be modified on the basis of culture results or presumed site of origin.

benzylpenicillin 2.4 g intravenously, 4 to 6-hourly
TOGETHER WITH EITHER
metronidazole 500 mg intravenously, 8 to 12-hourly (infused over 20 minutes)
OR
chloramphenicol* 750 mg to 1 g intravenously, 6-hourly

The duration of treatment depends on clinical response and radiological evidence of resolution.

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* In children refer to chloramphenicol dosage and comments under treatment of *Haemophilus influenzae* type b meningitis (p. 53).

SUBDURAL EMPYEMA AND EPIDURAL ABSCESS

In some instances, these infections may have a similar cause to brain abscess. However, subdural empyemas often follow trauma or neurosurgery and epidural abscesses are frequently associated with adjacent osteomyelitis, and therefore are more likely to be caused by a single organism. *Staphylococcus aureus* infection is more common in these conditions. Treatment should be based on the Gram stain and culture results of material obtained by aspiration or drainage. If delay is expected in obtaining such material, substitute (flu)cloxacillin for penicillin in the brain abscess regimen.

GENITAL TRACT INFECTIONS

URETHRITIS

Chlamydia trachomatis is now the commonest cause of urethritis. *Neisseria gonorrhoeae* is the other known important cause. In up to 50% of cases no pathogen is isolated. Treatment should be based wherever possible on the results of Gram stain and Chlamydial antigen detection. Patients with gonorrhoea should be treated for frequently coexisting non-gonococcal infection.

Gonococcal infection

ceftriaxone 250 mg intramuscularly, as a single dose
OR
spectinomycin 2 g intramuscularly, as a single dose
OR
ciprofloxacin 250 mg orally, as a single dose
EACH TOGETHER WITH
doxycycline 100 mg orally, 12-hourly for 10 days

This regimen is suitable for infections due to penicillinase-producing *N. gonorrhoeae* (PPNG) or likely to have been acquired in an area of high prevalence of PPNG (e.g. SE Asia, NSW, Victoria), or where the patient is hypersensitive to penicillin. If these criteria are not applicable then the following regimen may be used :

amoxycillin 3 g orally, with probenecid 1 g orally, both as a single dose
TOGETHER WITH
doxycycline 100 mg orally, 12-hourly for 10 days

Patients subsequently proven to have pharyngeal or ano-rectal infection should be given

ceftriaxone 250 mg intramuscularly, as a single dose

even if previously treated with another drug before culture results became available.

Sexual partners should be examined and treated appropriately. Because there are many regional differences in sensitivity of organisms and recommended treatments, post-treatment follow-up of the patient is recommended. A local expert in venereology should be consulted if in doubt or for complicated or disseminated infections.

Chlamydial and other non-gonococcal infection

doxycycline 100 mg orally, 12-hourly for 10 days

A second course, together with further investigation of the aetiology may be required if the symptoms persist or recur. Sexual partners of males with non-gonococcal urethritis should also be treated empirically to prevent recurrence in the male and to guard against chlamydial salpingitis developing in the female.

VAGINITIS

Most vaginitis is not sexually transmitted. The commonest pathogen is *Candida albicans*. Bacterial vaginosis is also common. The results of Gram stain and wet preparation can be used to guide therapy.

Candida albicans

Many effective topical preparations are available (amphotericin, clotrimazole, econazole, isoconazole, miconazole, nystatin). The following regimens are two of many that have been shown to be effective.

clotrimazole vaginal tablet (500 mg), as a single dose
OR
nystatin pessaries (each containing 100,000 Units), one inserted high into the vagina once daily for 7 days. Alternatively, nystatin vaginal cream (100,000 Units per 4g) inserted once daily for 7 days.

Bacterial vaginosis

This is the best term to describe a condition associated with malodorous vaginal discharge, paucity or absence of lactobacilli and overgrowth of *Gardnerella vaginalis*, and/or Mobiluncus species in association with other anaerobes.

metronidazole 400 mg orally, with food, twice daily for 7 days
OR
tinidazole 500 mg orally, with food, daily for 7 days
OR
amoxycillin 500 mg orally, 8-hourly for 7 days (preferable if treatment is required in pregnancy but less effective than metro/tinidazole).

Trichomonas vaginalis

tinidazole or metronidazole 2g orally, with food with food for 7 days as a single dose
OR
clotrimazole 100 mg vaginal tablets once daily for 6 days (may be preferable if treatment is required during pregnancy).

Treatment of partner(s) is indicated as this infection is usually sexually-transmitted.

PELVIC INFLAMMATORY DISEASE

Pelvic infection in females can either be sexually-acquired or result from mechanical interruption of the normal cervical barrier (e.g post-abortal, puerperal, post-operative or in association with an intra-uterine device). Infection is usually caused by mixed pathogens taking origin from vaginal flora, including anaerobes, facultative bacteria and sometimes *Mycoplasma hominis* and *Ureaplasma urealyticum*. When sexually-acquired, infection is initiated by *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae*. Depending on the initiating factors, treatment is designed to cover this broad range of pathogens.

Sexually-acquired infection

Mild infection (treated as an outpatient)

doxycycline 100 mg orally, 12-hourly for 14 days
TOGETHER WITH EITHER
metronidazole 400 mg orally, 12-hourly with food, for 14 days
OR
tinidazole 500 mg orally, daily, with food, for 14 days

Where penicillinase-producing *Neisseria gonorrhoeae* (which are often tetracycline-resistant) are suspected or proven, metronidazole should be replaced by:

amoxycillin/potassium clavulanate 500/125 mg orally, 8-hourly for 14 days

Severe infection (treated in hospital)

cefoxitin 2g intravenously, 8-hourly
TOGETHER WITH
doxycycline 100 mg orally, 12-hourly

until there is substantial clinical improvement, when the oral regimen above can be used for the remainder of 14 days.

If the patient is pregnant or breastfeeding, doxycycline should be replaced by

erythromycin 500 mg intravenously, 6-hourly or 500 mg orally, 6-hourly

Infection not sexually-acquired

It is vital that any intra-uterine device or retained products of conception be removed at or before the start of treatment.

Mild infection

amoxycillin 500 mg orally, 8-hourly for 10 days
TOGETHER WITH EITHER
metronidazole 400 mg orally, 12-hourly with food for 10 days
OR
tinidazole 500 mg, orally, with food, daily for 10 days

Severe infection

(amoxy)ampicillin 1 g intravenously, 6-hourly
TOGETHER WITH
metronidazole 500 mg intravenously, 12-hourly
OR
cefoxitin 2 g intravenously, 8-hourly as a single drug

until there is substantial clinical improvement, when the oral regimen above can be used for the remainder of 14 days.

If septicaemia is suspected, gentamicin should be added to the regimen. (refer to section on empirical therapy of septicaemia from the female genital tract, p. 47).

If infection with *Streptococcus pyogenes* or *Clostridium perfringens* is suspected or proven, then

benzylpenicillin 2.4 g intravenously, 4-hourly is the drug of choice

GONOCOCCAL OPHTHALMIA IN NEONATES

Untreated gonococcal conjunctival infection is highly contagious and may rapidly lead to blindness. Topical antimicrobial treatments are not sufficient and are not required when appropriate systemic antimicrobial therapy is given.

ceftriaxone 25-50 mg/kg/day, intravenously, as a single dose for 7 days
OR
cefotaxime 50-100 mg/kg/day, intravenously, in 2 divided doses for 7 days

In areas where the prevalence of penicillinase-producing *Neisseria gonorrhoeae* is low or where the organism from the neonate or mother is not a penicillinase-producer use

benzylpenicillin 60 mg/kg/day intravenously, in 4 divided doses, 6-hourly for 7 days

NEONATAL INCLUSION CONJUNCTIVITIS (caused by *C. trachomatis*)

Gram stain and culture should be done to exclude *N. gonorrhoeae*.

erythromycin syrup 50 mg/kg/day, in 4 divided doses, for 14 days

There is no evidence that topical therapy provides additional benefit. If conjunctivitis recurs after therapy, erythromycin treatment should be re-instituted for an additional 14 days.

SYPHILIS

Early syphilis (primary, secondary or latent syphilis of not more than two years duration)

For patients NOT hypersensitive to penicillin

procaine penicillin 1 g intramuscularly, daily for 10 days

Recent evidence suggests that in approximately 30% of cases of early syphilis *Treponema pallidum* can be isolated from CSF. This implies that the previous alternative recommendation of single dose benzathine penicillin 1.8 g intramuscularly may be inadequate and should only be given if follow-up is very difficult or unlikely.

For patients hypersensitive to penicillin

doxycycline 100 mg orally, 8-hourly for 15 days
OR
erythromycin 500 mg orally, 6-hourly for 15 days

Neither has good CSF penetration, but in the absence of new data, these must remain the recommended alternatives.

Late syphilis

Latent syphilis of more than two years or indeterminate duration

Treatment should be extended to 15 days for penicillin and 30 days for doxycycline/erythromycin.

Cardiovascular and neurosyphilis

Treatment should be extended to 20 days. In cardiovascular or neurosyphilis, concomitant treatment with prednisolone 20 mg orally, 12-hourly should be administered initially with penicillin to prevent a Herxheimer reaction. For neurosyphilis, a more intensive regimen may be necessary e.g.

benzylpenicillin 600 mg intravenously, 4-hourly for 15 days.

Pregnancy and congenital syphilis

Pregnant patients should be treated with penicillin in the dosage schedule recommended for non-pregnant patients at a similar stage of the disease. If allergic to penicillin such patients should receive erythromycin in the dosage appropriate to the disease. Tetracyclines should not be used in this group. Where a pregnant patient receives treatment with an agent other than penicillin, consideration should be given to investigating and treating the newborn.

GENITAL ULCER

Herpes simplex causes the great majority of the genital ulceration seen in our community at present. Currently available therapy is not curative, but acyclovir offers some relief or symptomatic improvement.

Herpes simplex

Primary infection

Systemic treatment is warranted in patients with severe primary herpes genitalis

acyclovir 200 mg orally, 5 times daily for 5 days

Recurrent infection

Suppressive treatment of recurrent infection is warranted only in patients who suffer very frequent recurrences (6 or more attacks in 6 months). Relapse is likely at the cessation of prophylaxis. In these cases use:

acyclovir 200 mg orally, 12-hourly for 6 months

Granuloma inguinale (Donovanosis)

doxycycline 100 mg orally, 12-hourly for 21 days

If the patient is pregnant or breastfeeding

erythromycin 500 mg orally, 6-hourly for 21 days

Uncommon causes

Uncommon but important causes of genital ulceration include primary syphilis, chancroid and granuloma inguinale. If any of these are suspected, referral to an STD specialist is recommended. Treatment for syphilis and granuloma inguinale is listed above.

GENITAL LUMP

Warts

Warts may be removed by chemical or physical means, or by surgical removal. Treatment needs to be individualised. For small numbers of readily accessible lesions the simplest treatment is

podophyllin 25% solution in tinc. benz. co. or absolute alcohol, applied with a cotton wool swab to each wart, and washed off in 4 hours. Application should be repeated twice weekly until the warts disappear. The normal skin surrounding the wart should be spared as much as possible.

Do not use this treatment in pregnancy, on cervical, meatal or ano-rectal warts.

The known association between genital warts and carcinoma of the cervix means that all women with warts should be referred for colposcopy. This should also apply to female partners of males with warts.

Molluscum contagiosum

These lesions are caused by a pox virus. In some cases, lesions may resolve spontaneously. The simplest treatment is to:

deroof aseptically with a needle or sharp, pointed stick, and express contents

Alternative treatments, as suggested for warts, are also suitable.

GENITAL ITCH

Scabies

lindane (gamma benzene hexachloride) 1% lotion, applied to the whole body from the neck down, left for 24 hours and then thoroughly removed by showering. In children, substitute benzyl benzoate 25% in place of lindane.

Underwear and bedclothes should be well washed. Treatment may be repeated at one week.

Pubic lice

lindane, as for scabies, but applied only to the affected area
OR
pyrethrins/piperonyl butoxide foam or shampoo, applied to the affected area, left overnight, and thoroughly washed off the next day.

Underwear and bedclothes should be well washed. Treatment may be repeated at one week.

PROSTATITIS

Prostatitis comprises two distinct clinical syndromes - acute and chronic prostatitis.

Acute prostatitis presents with lower urinary tract symptoms associated with fever, systemic symptoms, perineal pain and exquisite prostatic tenderness. Urinary tract pathogens are usually involved, although sexually transmitted pathogens may occasionally cause the condition. Most antibiotics penetrate well into the inflamed prostate and initial treatment is aimed at a broad range of pathogens and the prevention of bacteraemia.

In contrast, chronic prostatitis is notoriously difficult to diagnose as there is little inflammation present and the gland is normal on clinical examination. It should be suspected in patients with recurrent lower urinary tract infection. Few antibiotics penetrate into the non-inflamed prostate. Long term treatment in required, but even then is only effective in curing about one third of cases.

Acute prostatitis

(amoxy)ampicillin 1 g intravenously, 6-hourly
TOGETHER WITH
gentamicin 1 to 1.5 mg/kg intravenously, 8-hourly

until substantial clinical improvement when therapy can be changed to an appropriate oral agent, based on sensitivity of pathogen(s) isolated, for the remainder of 14 days. For milder infection, oral treatment utilising the multiple dose regimens for urinary tract infections may be suitable.

Chronic prostatitis

norfloxacin 400 mg orally, 12-hourly for 1 month
OR
ciprofloxacin 500 mg orally, 12-hourly for 1 month
OR
trimethoprim 300 mg orally, daily for 1 month

EPIDIDYMO-ORCHITIS

Apart from mumps, acute epididymo-orchitis is usually caused by sexually transmitted pathogens in males under 30 years old and by urinary tract pathogens in patients over 30 years old.

Patients less than 30 years old

Agents used are similar to those used for urethritis

amoxycillin 500 mg orally, 8-hourly for 10 to 14 days
TOGETHER WITH
doxycycline 100 mg orally, 12-hourly for 10 to 14 days

Where infection is due to penicillinase-producing *N. gonorrhoeae* (PPNG) or likely to have been acquired in an area of high prevalence of PPNG (e.g. S.E. Asia, N.S.W., Victoria), amoxycillin should be replaced by:

amoxycillin/potassium clavulanate 500 mg/125 mg orally, 8-hourly

In patients hypersensitive to penicillins

ciprofloxacin 500 mg orally, 12-hourly for 10 to 14 days

Patients more than 30 years old

amoxycillin 500 mg orally, 8 hourly
OR
cephalexin 500 mg orally, 6-hourly
OR
trimethoprim 300 mg orally, daily
OR
amoxycillin/potassium clavulanate 500 mg/125 mg orally, 8-hourly

Patients with systemic symptoms should be treated with intravenous therapy using the same agents as for acute prostatitis. Treatment should be continued for 10 to 14 days.

NON-SURGICAL ANTIBIOTIC PROPHYLAXIS

Prevention of Recurrent Rheumatic Fever

Continuous antimicrobial prophylaxis is recommended for patients with a well-documented history of rheumatic fever.

phenoxymethylpenicillin 250 mg orally, twice daily for some years

If patient compliance is likely to be poor, long-acting benzathine penicillin 900 mg intramuscularly, at intervals of 3 to 4 weeks, is an effective alternative. A possible disadvantage of benzathine penicillin is that any allergic response is likely to be protracted.

For patients hypersensitive to penicillin

erythromycin 250 mg orally, twice daily

Prevention of Meningitis Caused by *Neisseria meningitidis* and *Haemophilus influenzae* Type B

See Central Nervous System Infections, p. 53.

Prevention of Tuberculosis

For recent tuberculin converters or children with strongly positive tuberculin reactions

isoniazid 300 mg (10 mg/kg in children) orally, daily for 12 months

To prevent reactivation in persons with inactive tuberculosis who are immunosuppressed (e.g. receiving long-term corticosteroids, immunosuppressive or cytotoxic drugs, or radiotherapy)

isoniazid 300 mg orally, daily for 12 months

In certain circumstances, isoniazid alone may not be sufficient. Further information is available in the publication of the Commonwealth Department of Community Services and Health: Tuberculosis in Australia and New Zealand, 7th Ed., 1990. Australian Government Publishing Service, Canberra.

Prevention of Endocarditis or Infection of Prosthetic Implants

The case for antibiotic prophylaxis in patients with valvular heart disease, prosthetic valve implants and certain cardiac abnormalities (e.g. mitral valve prolapse with murmur) undergoing procedures that may cause transient bacteraemia is accepted, although not proven. For other implants, such as total hip replacement, the evidence supporting prophylaxis is even less definitive. However, if the patient is immunosuppressed, extensive surgery is required or established infection is present, then prophylaxis should be administered. The recommendations that follow call for fewer doses than previously, a trend supported by many authorities.

For patients having dental procedures, oral surgery or upper respiratory tract surgery

If the patient is NOT receiving long-term penicillin

amoxycillin 3 g orally, 1 hour before the procedure

If the patient is to have general anaesthesia (no prosthetic valve)

(amoxy)ampicillin 1 g intravenously, just before the procedure commences or intramuscularly, 30 minutes before the procedure commences, followed by 500 mg intravenously, intramuscularly or orally, 6 hours later

For patients hypersensitive to penicillin or patients receiving long-term penicillin

erythromycin 1.5 g orally, 1 to 2 hours before the procedure, followed by 500 mg orally, 6 hours later

OR

vancomycin 1 g intravenously, slowly over 1 hour, the infusion ending just before the procedure commences

For high-risk patients (e.g. patients with prosthetic valves or patients who have had a previous attack of infective endocarditis) having dental procedures, oral surgery or upper respiratory tract surgery; also for patients having gastrointestinal or genito-urinary procedures

(amoxy)ampicillin 1 g intravenously, just before the procedure commences or intramuscularly, 30 minutes before the procedure commences, followed by 500 mg intravenously, intramuscularly or orally, 6 hours later
TOGETHER WITH
gentamicin 1.5 mg/kg intravenously, just before the procedure commences or intramuscularly, 30 minutes before the procedure commences

Patients hypersensitive to penicillin

vancomycin 1 g intravenously, slowly over 1 hour, the infusion ending just before the procedure commences
FOLLOWED BY
gentamicin 1.5 mg/kg intravenously, just before the procedure commences

This regimen may not be satisfactory for all patients, e.g. those with renal impairment, clinical infection or prolonged labour. In such cases, a clinical microbiologist or infectious disease physician should be consulted.

Cardiac catheterisation, pacemaker insertion or skin biopsy

Prophylaxis is required for patients with prosthetic valves

(flu)cloxacillin 1 g intravenously
TOGETHER WITH
gentamicin 1.5 mg/kg intravenously, just before the procedure commences

These antibiotics may be given in the same doses intramuscularly, 30 minutes before the procedure.

Other Examples of Non-surgical Antibiotic Prophylaxis

Chemoprophylaxis may rarely be considered in many other situations e.g. staff who have been exposed to the infectious agent during the care of a patient with diphtheria, tuberculosis, typhoid fever, syphilis or Human Immunodeficiency Virus infection. In general, chemoprophylaxis is not advised and the problem should be discussed with a clinical microbiologist or infectious disease physician.

SURGICAL ANTIBIOTIC PROPHYLAXIS

INTRODUCTION

One-third to one-half of all antibiotics used in hospital practice are for surgical prophylaxis. Recent studies have shown levels of inappropriate use ranging from 30 to 90%, especially with respect to the timing and duration.

Where a prophylactic regimen is marked with an asterisk (*), there is general acceptance of its value. For the remainder, prophylaxis is controversial and may not be indicated if a surgical team has a low infection rate for that procedure in a particular institution.

Adherence to the following principles will enable the potential benefit of surgical antibiotic prophylaxis to be realised while minimising adverse effects.

PRINCIPLES

Definition

Prophylaxis, the use of antibiotics before infection takes place e.g. in elective colonic resection, must be distinguished from their use in **early treatment,** where infection is already established although not necessarily evident pre-operatively, e.g. removal of a perforated appendix.

Indication

Prophylaxis should be considered where there is a high risk of infection e.g. colonic resection, or where post-operative infection, even if uncommon, would have severe consequences e.g. infection associated with a prosthetic implant.

Causative Organisms

In general, antimicrobials should be directed against the likely causative organism(s); however, an effective prophylactic or early treatment regimen need not necessarily include antibiotics that are active against every potential pathogen.

Regimens that only decrease the total number of organisms may assist host defences and prevent infection. Most post-surgical infections are due to the patient's own organisms which, in hospitalised patients, may include multiresistant organisms. Accordingly the following recommendations may need to be modified. The choice of antimicrobial agents should take into account the organisms causing infections within the institution and their patterns of sensitivity.

Aim

The route of administration, timing and duration of prophylactic antibiotics should be chosen **to achieve high plasma and tissue levels of the drug(s) during and shortly after the surgical procedure** when bacterial contamination is maximal.

Route of Administration

This is usually parenteral, either intravenous or intramuscular, but in certain instances rectal or oral administration may be appropriate.

Timing

Intravenous antibiotics require administration immediately after induction of anaesthesia. This requires coordination with the anaesthetist and prior organisation to ensure that drugs are available in theatre. Intramuscular antibiotics should be given at the time of premedication for surgery. Rectally administered metronidazole should be given 2 to 4 hours before surgery and oral tinidazole, 6 to 12 hours prior to surgery.

Duration

Animal work clearly shows that the critical period for successful prophylaxis lies in the 4 hours following implantation of organisms into a wound. **In general, a single dose of a parenteral drug may be sufficient.** However, if prophylactic antibiotics have been

administered in the ward or emergency department, unexpected variation in scheduling patients for theatre can result in sub-optimal levels of drug at the time of surgery. Under these circumstances the pre-operative dose should be supplemented by a further dose administered at the time of operation. Equally, if surgery is prolonged, a second dose should be given. Post-operative administration of prophylactic drugs is usually unnecessary and may be harmful. **Continuation of therapy for more than 1 to 2 doses is not advised unless it is being given specifically as early treatment for established infection or where indicated in the tables on p. 79 to 83. The practice of continuing prophylactic antibiotics until such time as surgical drains have been removed is both illogical and unproven.**

Topical Antibiotics

With the exception of ophthalmic surgery, burns or extensive skin loss, topical antibiotic prophylaxis is not recommended.

Protocols

Prophylactic or early treatment regimens should be agreed, implemented and adhered to by surgeons within a given institution. Chosen regimens should be reviewed on a regular basis but only varied if their effectiveness (based on the infection rate for a given procedure) is in question, or if verified data on an alternative regimen suggest that a more appropriate choice can be made (on the grounds of efficacy, cost, toxicity or ease of administration).

INDICATIONS FOR SURGICAL ANTIBIOTIC PROPHYLAXIS

Cardiac Surgery

Conclusive evidence, based on controlled trials, in this area is lacking; however, prophylaxis is commonly given when prostnetic heart valves are inserted.* The usefulness of prophylactic antibiotics in coronary artery bypass surgery has not been established and the infection rate for this procedure in a given institution should be considered when deciding whether prophylaxis is to be used.

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*General acceptance of value

Arterial Reconstructive Surgery

Surgery involving the abdominal aorta and/or the lower limb, particularly if a groin incision is involved,* may benefit from prophylactic antibiotics. Patients undergoing any vascular procedure involving a prosthesis should probably also receive prophylaxis. The incidence of infection after operations on the brachial and carotid arteries, not involving prosthetic materials, is too low to justify the use of prophylactic antibiotics.

Orthopaedic Surgery

Prophylaxis should be given for prosthetic large joint replacement. A decrease in the infection rate has been demonstrated for proximal femoral fractures treated with internal fixation under appropriate anti-staphylococcal antibiotic cover.

It may also be appropriate to use prophylactic antibiotics for other orthopaedic procedures involving insertion of prosthetic or transplant material but this remains unproven.

The value of incorporating antibiotic into cement for primary or non-infected joint insertion is unproven but it has been used successfully in the replacement of infected joint prostheses.

It is recommended that antibiotic prophylaxis be given when there is severe musculoskeletal and soft tissue trauma, including compound fractures.* In this situation, an increased duration of therapy (early treatment) may be appropriate.

Neurosurgery

With the exception of cerebrospinal fluid leakage following trauma, and craniotomy involving the implantation of prosthetic material, e.g. shunts, prophylactic antibiotic use remains unproven.

Head, Neck and Thoracic Surgery (including Ear, Nose, Throat and Dental Procedures)

Prophylaxis should in general be considered for procedures that involve an incision through oral, nasal, pharyngeal or oesophageal mucosa, stapedectomy or similar operations, or the insertion of prosthetic material. Use of antibiotic prophylaxis for tonsillectomy

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*General acceptance of value

and adenoidectomy is unproven. Where an established focus of infection is suspected or shown to be present, e.g. chronic mastoiditis, an early treatment regimen is appropriate.

Gastrointestinal Surgery

When the stomach or duodenum is to be opened, prophylaxis should be considered if the mechanisms that normally inhibit bacterial growth in the stomach and duodenum, namely gastric acidity and gastrointestinal motility, are diminished by conditions such as obstruction, haemorrhage, gastric ulceration, gastric malignancy, previous gastric surgery (e.g. vagotomy, gastrectomy) or drugs reducing gastric acidity e.g. cimetidine.

Endoscopic procedures

Endoscopic **procedures** may be divided into high risk procedures (sclerotherapy, oesophageal dilatation, sphincterotomy, ERCP, endoscopy with biopsy) or low risk procedures (e.g. endoscopy without biopsy). Similarly **patients** may be divided into high risk patients (those with prosthetic cardiac valves, previous endocarditis or rheumatic valvular disease) and low risk patients, (no cardiac disease, mitral valve prolapse, ASD, pacemaker). Prophylaxis is necessary for high risk procedures and/or high risk patients.* The need for prophylaxis diminishes and is unnecessary for most low risk procedures in low risk patients.

Biliary Tract Surgery

Prophylaxis should generally be considered only for patients at increased risk of acquiring infection, e.g. those: (i) older than 70 years; (ii) with acute cholecystitis; (iii) in whom complicated surgery or re-operation is to be undertaken; or (iv) having surgery involving the common bile duct, particularly in the presence of obstruction, where anaerobic organisms are more likely to be present.

Colorectal Surgery

The measures that can be taken to reduce the high risk of infection associated with colorectal surgery are not equally applicable to both elective and emergency procedures.

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* General acceptance of value

1. Elective Procedures - Mechanical bowel preparation pre-operatively, with appropriate peri-operative antibiotic(s) administered parenterally, rectally or orally have been shown to substantially reduce infective complications. Marked improvement accompanies use of drugs active against *Bacteroides fragilis*,* however additional protection results if aerobic Gram-negative cover is also provided by an aminoglycoside or ß-lactam.

2. Emergency Procedures - Mechanical bowel preparation is not possible and parenterally administered antibiotics are recommmended.* If obvious peritonitis is detected at surgery or if major peritoneal soiling occurs, then an early treatment regimen should be adopted.

Appendicectomy

The ideal regimen is not yet established. One approach is to give all patients pre-operative prophylaxis (e.g. metronidazole rectally at the time of rectal examination) and decide at operation whether further doses are necessary, e.g. if the appendix is perforated. Alternatively, the decision to give prophylaxis can be made when the appendix is inspected. A gangrenous, perforated, severely inflamed or complicated appendix requires a longer duration of therapy* (see also, peritonitis, p. 36).

Penetrating Abdominal Wounds

The two approaches outlined for appendicectomy are appropriate for this situation.

Obstetric and Gynaecological Surgery

Antibiotic prophylaxis has been shown to decrease the incidence of septic complications following Caesarean section in high risk patients, e.g. those in labour or with ruptured membranes. To avoid exposing the infant to the drug, administration can be delayed until after the cord is clamped. Infective complications following hysterectomy, particularly if performed by the vaginal route, can also be reduced by appropriate prophylaxis. An infected abortion requires appropriate early treatment.

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* General acceptance of value

Urological Surgery

Prophylaxis is not usually recommended for patients with sterile urine at the time of urological surgery. Patients suspected of having urinary tract infection should be treated pre-operatively to prevent post-operative sepsis and ideally this should be on the basis of prior urine culture, with therapy being guided by sensitivity results. Strict maintenance of closed-catheter drainage can prevent urinary tract infection in patients who temporarily require an indwelling catheter; use of neomycin-polymyxin irrigants does not provide any additional benefit and may select resistant organisms. Equally, administration of oral antibiotics to cover the period of catheterisation is not recommended.

Lower Limb Amputation

Amputation, particularly of an ischaemic leg,* carries a small but important risk of clostridial infection. Appropriate antibiotic prophylaxis must be given.

Simple lacerations

Several studies have found that prophylactic antibiotics do not decrease the incidence of infection in this situation.

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* General acceptance of value

SURGICAL ANTIBIOTIC PROPHYLAXIS

Nature of Operation	Likely Pathogens	#Recommended Regimen (usually 1 to 2 doses only)
CLEAN		
Cardiovascular		
Prosthetic valve*	*Staphylococcus aureus*, *Staphylococcus epidermidis*, diphtheroids, aerobic Gram-negative bacilli	(flu)cloxacillin 2 g IV *TOGETHER WITH* gentamicin 1.5 mg/kg IV *OR* (as a single agent) cephalothin 2 g IV
Arterial reconstructive surgery involving a prosthesis AND groin incision*	*Staphylococcus aureus*, aerobic Gram-negative bacilli	as above
Orthopaedic		
Joint replacement,* internal fixation of selected fractures	*Staphylococcus aureus*, *Staphylococcus epidermidis*	(flu)cloxacillin 2 g IV *OR* cephalothin 2 g IV
Neurosurgery		
CSF leakage	*Streptococcus pneumoniae*	procaine penicillin 1 g IM, followed by phenoxymethylpenicillin 500 mg orally, 6-hourly until dry
Craniotomy involving prosthetic implants	*Staphylococcus aureus*, *Staphylococcus epidermidis*, diphtheroids	(flu)cloxacillin 2 g IV

* General acceptance of value. In the absence of an asterisk, prophylaxis may not be indicated.
#Other regimens taking into account likely pathogens. toxicity and cost may be equally rational.

Nature of Operation	Likely Pathogens	Recommended Regimen (usually 1 to 2 doses only)
CLEAN CONTAMINATED		
Head, Neck and Thoracic		
Involving oral, pharyngeal or oesophageal mucosa	Mixed aerobic and anaerobic upper respiratory tract flora	benzylpenicillin 600 mg IV
Extensive procedures particularly for carcinoma	As above plus *Staphylococcus aureus* and aerobic Gram-negative bacilli	cephalothin 2 g IV
Gastroduodenal		
Incision into lumen with predisposing factors	Aerobic Gram-negative bacilli, Streptococci, *Enterococcus faecalis* and some anaerobic bacteria	(amoxy)ampicillin 1 g IV (as a single agent) *OR* cephalothin 2 g IV *TOGETHER WITH* metronidazole 500 mg IV
Endoscopic procedures		
a) High risk procedures and/or patients*	As above	(amoxy)ampicillin 1 g IV or IM *PLUS* gentamicin 1.5 mg/kg IV or IM
b) High risk procedures and/or patients if hypersensitive to penicillin*	As above	vancomycin 1 g IV, slowly over 1 hour *PLUS* gentamicin 1.5 mg/kg IV or IM
c) Low risk patients and/or procedures	As above	(amoxy)ampicillin 1 g IV or IM

* General acceptance of value. In the absence of an asterisk, prophylaxis may not be indicated.
# Other regimens taking into account likely pathogens, toxicity and cost may be equally rational.

Nature of Operation	Likely Pathogens	Recommended Regimen (usually 1 to 2 doses only)
CLEAN CONTAMINATED		
Biliary Tract		
Those with predisposing factors (see p. 76)	Aerobic Gram-negative bacilli, *Enterococcus faecalis*. If obstruction present, also anaerobic bacteria	(amoxy)ampicillin 1 g IV *PLUS* gentamicin 1.5 mg/kg IV *OR* (or as a single agent) cephalothin 2 g IM or IV
Colorectal		
Elective*	Anaerobic bacteria, Streptococci, *Enterococcus faecalis*. aerobic Gram-negative bacilli	tinidazole 2 g orally, 6 to 12 hours previously *OR* metronidazole 1 g rectally, 2 to 4 hours previously *TO WHICH MAY BE ADDED* gentamicin 1.5 mg/kg IV
Emergency*	As above	gentamicin 1.5 mg/kg IV *TOGETHER WITH EITHER* metronidazole 500 mg IV *OR* clindamycin 600 mg IV

* General acceptance of value. In the absence of an asterisk, prophylaxis may not be indicated.
# Other regimens taking into account likely pathogens, toxicity and cost may be equally rational.

Nature of Operation	Likely Pathogens.	#Recommended Regimen (usually 1 to 2 doses only)
CLEAN CONTAMINATED		
Obstetrics and Gynaecology		
Hysterectomy	Anaerobic bacteria, aerobic Gram-negative bacilli, Streptococci	tinidazole 2 g orally, 6 to 12 hours previously *OR* metronidazole 1 g rectally, 2 to 4 hours previously
Caesarean section high risk only (see p. 77)	As above, but increased risk of aerobic Gram-negative organisms	cefoxitin 1 g IV (as a single agent) *OR* cephalothin 2 g IV *PLUS* metronidazole 500 mg IV
Urological		
For proven or suspected urinary infection	Aerobic Gram-negative bacilli, *Enterococcus faecalis* and Staphylococci	according to urine culture and sensitivity. If data unavailable, gentamicin 2 mg/kg IM or IV
Amputation		
Involving a lower limb for ischaemia*	*Clostridium perfringens*, *Staphylococcus aureus*, aerobic Gram-negative bacilli	benzylpenicillin 1.2 g IV, 6-hourly for 48 hours *OR* metronidazole 1 g rectally, or 500 mg IV, 12-hourly for 48 hours

* General acceptance of value. In the absence of an asterisk, prophylaxis may not be indicated.
#Other regimens taking into account likely pathogens, toxicity and cost may be equally rational.

Nature of Operation	Likely Pathogens	*Recommended Regimen (usually 1 to 2 doses only)
CONTAMINATED (EARLY TREATMENT)		
Ruptured, perforated or gangrenous viscus*		
e.g. perforated colon or appendix	Aerobic Gram-negative bacilli, anaerobic bacteria, *Enterococcus faecalis* and Streptococci	see management of peritonitis p. 36
Muscular, skeletal and soft tissue trauma*		
Particularly if severe, and/or with compound fractures	*Staphylococcus aureus*, *Streptococcus pyogenes*, *Clostridium perfringens*, aerobic Gram-negative bacilli	(flu)cloxacillin 1 g IV, 4-hrly *TOGETHER WITH* gentamicin 1.5 mg/kg IV, 8-hrly for 48 hours
MISCELLANEOUS (TOPICAL TREATMENT)		
Burns, extensive skin loss	*Staphylococcus aureus*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, aerobic Gram-negative bacilli	silver sulphadiazine with chlorhexidine, topically
Ophthalmic	*Staphylococcus aureus*, Streptococci, *Staphylococcus epidermidis*	chloramphenicol eye drops or ointment for 1 to 2 days only

* General acceptance of value. In the absence of an asterisk, prophylaxis may not be indicated.
#Other regimens taking into account likely pathogens, toxicity and cost may be equally rational.

GUIDELINES FOR GENERAL PRACTICE

General practitioners primarily see undifferentiated illness. Diagnostic uncertainty is common and clinical experience may be misleading. There is often patient pressure (and physician susceptibility) for a 'pill for every ill'. The prescription of antibiotics is usually empirical, with microbiological investigations properly reserved for patients who appear more seriously ill, or those who have failed to respond to previous therapy. Peer review has been infrequent. The major source of information concerning pharmaceuticals comes from commercial drug representatives.

Under these circumstances, it is understandable that surveys of Australian general practitioner antibiotic prescribing habits have shown the following:

1. Extensive use of broad-spectrum, rather than narrow-spectrum drugs, in situations where the latter drugs are efficacious.
2. The use of newer, more expensive, heavily promoted drugs in situations where older, more cost-effective medication is equally effective.
3. The use of antibiotics in conditions, such as acute bronchitis, where the etiology is primarily viral.

This section of the Guidelines has been substantially modified in the light of information received from 200 Victorian general practitioners who, in 1989, generously provided data concerning 14,500 antibiotic prescriptions to the Victorian Medical Postgraduate Foundation (VMPF).

The aim is to provide not only a reference booklet for difficult situations, but also a set of practical recommendations for common conditions, against which practitioners can review their own prescribing habits. In this regard, we welcome feedback concerning the issues involved.

FURTHER READING

CHECK programme of self-assessment, UNIT 202: Antibiotics. The Royal Australian College of General Practitioners, 1988.
Buchanan N, Baird-Lambert J. Prescribing medications for children. Williams & Wilkens and Associates Pty. Ltd. 1988 Sydney.

CONTENTS

RESPIRATORY TRACT INFECTIONS

Undifferentiated upper respiratory tract infection

This is a common diagnosis in febrile children, when otitis media and tonsillitis have been excluded. The etiological agents are invariably viral (usually rhinoviruses, sometimes respiratory syncitial virus, parainfluenza and influenza viruses). Most symptoms will subside in a few days although cough may persist for up to two weeks.

Antibiotics are not indicated,
If fever is significant, paracetamol is of value

Antibiotics are often prescribed to 'prevent' bacterial complications, such as otitis media but there is no evidence to justify this practice. Antihistamines and pseudoephedrine are of no value. The former can cause nightmares and daytime hyperactivity in young children. The usually self-limiting nature of the condition needs to be explained to parents, as does the need to return if the occasional bacterial secondary infection develops.

Acute sore throat

This is most often caused by viral infection. Diphtheria is now uncommon in Australia. Antibiotic therapy is warranted if infection with *Streptococcus pyogenes* is suspected or proven. A streptococcal etiology is more likely in children between the ages of 4 and 7 years, and in febrile patients with exudative tonsillitis and cervical lymphadenopathy.

phenoxymethylpenicillin 25 to 50 mg/kg/day (to a maximum adult daily dose of 1 g) orally, in 2 to 3 divided doses
OR
erythromycin 30 to 50 mg/kg/day (to a maximum adult daily dose of 1 g) orally, in 2 to 3 divided doses

Although symptoms and most evidence of this infection will disappear within 1 or 2 days of treatment, a full course of 10 days should be prescribed to give the best chance of eradicating *Streptococcus pyogenes* from the nasopharynx and thereby minimising the risk of recurrence or complications such as glomerulonephritis or rheumatic fever. Treatment may be initiated with one injection of procaine penicillin intramuscularly. In severe

disease, parenteral penicillin may be required for the initial 3 to 5 days and even longer in the treatment of quinsy.

Amoxycillin alone, or in combination with potassium clavulanate, SHOULD NOT BE USED as they have no advantage over penicillin and more commonly produce a rash, especially if the sore throat is due to glandular fever (infectious mononucleosis). Patients treated with co-trimoxazole have a greater incidence of bacteriological failure than those treated with penicillin.

Acute bacterial otitis media and sinusitis

Many children with viral upper respiratory tract infections have mild reddening or dullness of the ear drum and antibiotics are not warranted. In contrast, where the ear drum is red or yellow and bulging, with loss of anatomical landmarks, antibiotic therapy is indicated. Decongestants and antihistamines are often given in addition to antibiotic therapy in acute otitis media. Several controlled trials have not only failed to show a benefit from such additional therapy but have noted more adverse experiences, such as sleep disturbance, irritability, bad temper and hallucination. Their use is not recommended.

Common causative bacteria: *Streptococcus pneumoniae, Haemophilus influenzae. Branhamella catarrhalis* is less frequently isolated but is often amoxycillin-resistant. *Staphylococcus aureus* or anaerobes may sometimes be involved in acute sinusitis. However, the clinical outcome does not necessarily reflect *in vitro* susceptibility.

amoxycillin 25 to 75 mg/kg/day (to a maximum adult daily dose of 1.5 g) orally, in 2 to 3 divided doses, for 5 days

OR

trimethoprim 300 mg orally, 12-hourly for 5 days (until a paediatric suspension is available in Australia, co-trimoxazole may be substituted in children)

OR

doxycycline 100 mg orally, 12-hourly for five days. For milder infections 100 mg orally, once daily may suffice (do not use in children or pregnant women)

OR

cefaclor 20 to 40 mg/kg/day (to a maximum adult daily dose of 2 g) orally, in 2 to 3 divided doses for 5 days

OR

amoxycillin/potassium clavulanate 40/10 mg/kg/day (to a maximum adult daily dose of 1500/375 mg) orally, in 3 divided doses for 5 days. This combination should not be preferred to amoxycillin alone unless resistance to amoxycillin is suspected or proven.

Acute epiglottitis

An uncommon but life-threatening cause of upper airway obstruction which is seen mainly in children but may occur in adults. Urgent hospitalisation is required. (see p. 16).

Croup (acute laryngotracheobronchitis)

Croup is caused by parainfluenza viruses, but may also be due to respiratory syncitial virus, rhinoviruses and the measles virus. It is usually preceded by a coryzal illness, as opposed to acute epiglottis, which has a rapid onset. The illness is self-limiting and lasts 2 to 7 days. Antibiotics are not indicated

If severe (e.g. sternal retraction at rest) refer to hospital.

Acute bronchitis

This diagnosis is one of the commonest indications for prescribing antibiotics. Yet, in a previously healthy person, the etiology is most often viral. Antibiotics are only indicated if the course of acute bronchitis is protracted or severe. Under these circumstances, secondary bacterial infection should be assumed, usually due to *Streptococcus pneumoniae* or *Haemophilus influenzae*.

amoxycillin 25 to 75 mg/kg/day (to a maximum adult daily dose of 1.5 g) orally, in 2 to 3 divided doses for 5 days

OR

doxycycline 200 mg orally, as a loading dose, then 100 mg orally, daily for 5 days (do not use in children or pregnant women)

OR

erythromycin 30 to 50 mg/kg/day (to a maximum adult daily dose of 1.5 g) orally, in 3 divided doses

If *Mycoplasma pneumoniae* infection is suspected on epidemiological grounds, amoxycillin is inappropriate.

Acute exacerbations of chronic bronchitis

While the etiology of this condition may be viral, important causative bacteria are *Streptococcus pneumoniae* and *Haemophilus influenzae; Branhamella catarrhalis* is less frequently involved but is commonly amoxycillin resistant. Clinical outcome is not necessarily predicted by *in vitro* sensitivity.

amoxycillin 750 mg orally, 12-hourly
or 500 mg orally, 8-hourly for 5 days

OR

trimethoprim 300 mg orally, 12-hourly for 5 days

OR

doxycycline 100 mg orally, 12-hourly for 5 days (do not use in children or pregnant women)

OR

amoxycillin/potassium clavulanate (250/125 mg) orally, 8-hourly for 5 days. This combination should not be preferred to amoxycillin alone unless resistance to amoxycillin is proven, or suspected because of lack of response or recurrence.

Influenza

Antibiotics are not indicated in a previously healthy person. In those at special risk (e.g. chronic heart or lung disease, the elderly or in pregnant women), secondary bacterial infection may require treatment as for acute bronchitis (see p. 16).

Pneumonia

Treatment will frequently have to be initiated for a patient with the clinical and X-ray features of pneumonia before a bacteriological diagnosis can be confirmed.

Pneumonia in previously healthy adults and children

The predominant bacterial pathogen is *Streptococcus pneumoniae*.

If not severe, as for acute exacerbations of chronic bronchitis (see above)

OR

procaine penicillin 1.5 g intramuscularly, daily for 5 days

In patients hypersensitive to penicillin, erythromycin may be used as in the regimen given for Atypical Pneumonia.

Primary atypical pneumonia

May be seen in Mycoplasma and Legionella infections, Psittacosis or Q fever. Often occurs in previously healthy subjects.

doxycycline 100 mg orally, 12-hourly for 7 to 10 days
(Recommended if Psittacosis or Q fever is suspected, satisfactory for Mycoplasma)
OR
erythromycin 500 mg orally, 6-hourly for 7 to 10 days
(Recommended if Legionella infection is suspected, satisfactory for Mycoplasma).

URINARY TRACT INFECTIONS

Antimicrobial therapy of urinary tract infections is assisted by a high fluid intake, complete bladder emptying, and in some instances (e.g. if aminoglycosides are used), by alkalinisation of the urine e.g. by sodium citrotartrate 4 g orally, 6-hourly.

Acute uncomplicated urinary tract infection

The regimens recommended below can be expected to cure 80% to 90% of uncomplicated urinary tract infections. Treatment failures will usually be due either to a resistant organism or an unsuspected underlying abnormality of the urinary tract.

Single-dose therapy (not recommended in men, in whom underlying problems are common)

amoxycillin 3 g orally
OR
trimethoprim 600 mg orally
OR
gentamicin 120 mg intramuscularly

Multiple-dose therapy (5 day course)

amoxycillin 250 mg orally, 8-hourly
OR
trimethoprim 300 mg, daily
OR
cephalexin 250 mg orally, 6-hourly
OR

amoxycillin/potassium clavulanate (250/125 mg) orally, 8-hourly. This combination should not be preferred to amoxycillin alone unless resistance to amoxycillin is suspected or proven.

Neither co-trimoxazole or norfloxacin are recommended for the treatment of acute uncomplicated urinary tract infection. Trimethoprim alone is just as efficacious as co-trimoxazole, causes less side effects, and is cheaper. Norfloxacin has not been shown to produce better cure rates than alternative regimens for uncomplicated urinary infection, is very expensive, and should be reserved for more difficult situations.

Complicated urinary tract infection

Attempts should be made to define or exclude any underlying anatomical or functional abnormality.

The antibiotic sensitivities of organisms cultured from complicated urinary tract infections are often difficult to predict and it is important that adequate urine cultures are performed prior to commencing therapy. Consultation with your local pathology laboratory may assist in selecting the most appropriate therapeutic regimen, both for initial therapy and, if modification is required, when culture and sensitivity results become available. Drugs such as amoxycillin/potassium clavulanate or norfloxacin may be appropriate.

Recurrent or chronic urinary tract infections

Recurrent infections occur either as relapse of a previously treated infection or because of reinfection. In female patients, instruction on perineal hygiene, and micturition after intercourse may assist in preventing reinfection.

For the acute treatment of an episode of recurrent or chronic urinary infection give a 5 to 7 day course of

amoxycillin/potassium clavulanate (250/125 mg) orally, 8-hourly
OR
nitrofurantoin 50 to 100 mg orally, 6-hourly
OR
norfloxacin 400 mg orally, 12-hourly

Prophylaxis instituted after successful treatment can reduce or prevent subsequent attacks and may be continued for 3 to 6 months,

or on occasions longer. Appropriate prophylactic therapy is usually given at night, but may be taken by women after intercourse

nitrofurantoin 50 to 100 mg orally, nightly
OR
trimethoprim 150 mg orally, nightly

Catheter associated urinary infections

As a general rule, these should only be treated if the patient shows signs of systemic infection, eg fever, rigors or loin pain. If required, antibiotics should be selected on the basis of the most recent urine culture results. Removal of the catheter, whenever possible, makes the greatest contribution towards cure.

Prolonged or sequential courses of antibiotics given for the treatment of catheter-associated urinary tract infections, whilst the catheter remains in situ are usually unsuccessful and tend to select for organisms resistant to many antibiotics. For similar reasons, local irrigation with antibiotics should not be used.

If a catheter needs to be changed in the presence of proven urinary infection then this procedure should be preceded by a single dose of an appropriate antibiotic administered by the intramuscular or intravenous route. The choice should take into account the sensitivity of the current infecting organisms. If this information is not available, a single parenteral dose of gentamicin 2 mg/kg should be given 30 minutes before the procedure is undertaken.

SKIN, MUSCLE & BONE INFECTIONS

Impetigo

May resolve with topical antiseptic treatment, e.g. chlorhexidine or povidone-iodine. Topical antibiotics are not recommended. The organisms commonly encountered are *Streptococcus pyogenes*, *Staphylococcus aureus* or a mixture of the two. If an antibiotic is required:

(flu)cloxacillin 500 mg orally, 12-hourly for 10 days
OR
erythromycin 500 mg orally, 12-hourly for 10 days

Some strains of *Staphylococcus aureus* are resistant to erythromycin.

Boils, carbuncles and bullous impetigo

The causative organism is generally *Staphylococcus aureus*, occasionally in association with *Streptococcus pyogenes*.

If the lesions are small or few in number they may be managed by local antiseptics and drainage. If lesions are extensive or cause systemic symptoms an antibiotic is required:

(flu)cloxacillin 500 mg orally, 6-hourly
OR
erythromycin 500 mg orally, 12-hourly

Some strains of *Staphylococcus aureus* are resistant to erythromycin.

Cellulitis and erysipelas

1. *Streptococcus pyogenes* is classically the causative organism
   procaine penicillin 1 g intramuscularly, 12-hourly
   OR
   phenoxymethylpenicillin 500 mg orally, 6-hourly

If hypersensitive to penicillin

cephalexin 500 mg orally, 6-hourly
OR
erythromycin 500 mg orally, 12-hourly

2. *Staphylococcus aureus* - if suspected
   (flu)cloxacillin 500 mg to 1 g orally, 6-hourly
   OR
   cephalexin 500 mg orally, 6-hourly
   OR
   erythromycin 500 mg orally, 12-hourly

Suppurative wound infections (surgical or traumatic)

Local measures such as surgical drainage, irrigation with isotonic stabilised sodium hypochlorite solution*, saline dressings or use of a local antiseptic such as povidone-iodine usually suffice. Topical use of antibiotics may cause the emergence of resistant organisms and is not recommended.

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* Health Department Victoria. "Staphylococcal Infections in Hospitals", 3rd Ed., 1987, p. 22.

If there is surrounding cellulitis and/or systemic symptoms are present, treat as for staphylococcal cellulitis (see p. 29). If Gram-negative organisms are suspected or known to be involved, use cephalexin orally or cephalothin intravenously or gentamicin 1 to 1.5 mg/kg intravenously or intramuscularly, 8-hourly.

Varicose or decubitus ulcers

Local measures including those for suppurative wound infections are most important. If there is surrounding cellulitis, treat with systemic antibiotics (see p. 29). Where there is extensive tissue damage, anaerobic organisms are likely to be involved and

metronidazole 400 mg orally, 12-hourly should be added

Bites

Both animal and human bites commonly become infected with mouth flora. In animal bites *Pasteurella multocida* is commonly involved. Adequate wound toilet is important but even if overt infection is not present all bites should be treated with

phenoxymethylpenicillin 500 mg orally, 6-hourly for 5 days
OR
procaine penicillin 1 g intramuscularly daily, for 5 to 7 days

If severe infection is present or response to the above regimens is poor, parenteral treatment with other antibiotics or surgical drainage may be needed.

Diabetic foot infections

These should always be regarded as serious and treated vigorously (see p. 31).

ALIMENTARY TRACT INFECTIONS

Oral and Dental Infections

Causative organisms are usually mixed anaerobic and aerobic oral flora. In virtually all instances, referral to a dental surgeon is advisable to exclude or treat any underlying cause.

Gingival infections

In the absence of systemic signs or symptoms, antibiotic therapy is not usually indicated and local dental care to control bacterial plaque will often suffice. If accompanied by systemic signs or symptoms

procaine penicillin 1 g intramuscularly, daily for 5 days
OR
phenoxymethylpenicillin 500 mg orally, 6-hourly for 5 days
OR
metronidazole 200 to 250 mg orally, 8-hourly for 5 days

and refer for dental management. In severe cases both procaine penicillin and metronidazole may be required.

Pericoronitis or tooth abscess

In the absence of systemic signs or symptoms, antibiotic therapy is not usually indicated and local dental care will often suffice. In pericoronitis, vigorous warm mouth rinses with saline or 1:200 chlorhexidine and a topical paint e.g. povidone-iodine, helps greatly. In the case of a tooth abscess, removal of the infected pulp tissue, with or without drainage, is usually required. If accompanied by systemic signs or symptoms

procaine penicillin 1 g intramuscularly, daily for 3 days
OR (for the milder case)
phenoxymethylpenicillin 500 mg orally, 6-hourly for 2 to 3 days
OR (if unresponsive)
amoxycillin/potassium clavulanate (250/125 mg) orally, 8-hourly
OR (if hypersensitive to penicillin)
clindamycin 300 mg intravenously, 8-hourly or 300 mg orally, 8-hourly for 2 to 3 days

Oral candidiasis

Local cleaning care, especially beneath dentures, is of assistance.

amphotericin 1 lozenge (10 mg) dissolved slowly in the mouth, 6-hourly for 7 to 14 days
OR
nystatin 1 lozenge (100,000 units) dissolved slowly in the mouth, 6-hourly for 7 to 14 days.

Nystatin suspension may be used if the lozenge cannot be tolerated e.g. in infants.

Diarrhoeal Disease

There are many bacterial causes of diarrhoea such as enterotoxigenic *E. coli, Campylobacter jejuni,* Salmonella and Shigella species. In general, antibiotic therapy is not recommended in uncomplicated diarrhoeal diseases except in the following situations:

Acute giardiasis

tinidazole 2 g orally, as a single dose
OR
metronidazole 200 to 500 mg orally, 8-hourly for 5 days
OR
benzoyl metronidazole suspension 20 to 30 mg/kg/day orally, in 3 divided doses for 7 days

GENITAL TRACT INFECTIONS

Urethritis

Chlamydia trachomatis is now the commonest cause of urethritis. *Neisseria gonorrhoeae* is the other known important cause. In up to 50% of cases no pathogen is isolated. Treatment should be based wherever possible on the results of Gram stain and Chlamydial antigen detection. Patients with gonorrhoea should be treated for frequently coexisting non-gonococcal infection.

Gonococcal infection

ceftriaxone 250 mg intramuscularly, as a single dose
OR
spectinomycin 2 g intramuscularly, as a single dose
OR
ciprofloxacin 250 mg orally, as a single dose
EACH TOGETHER WITH
doxycycline 100 mg orally, 12-hourly for 10 days

This regimen is suitable for infections due to penicillinase-producing *N. gonorrhoeae* (PPNG) or likely to have been acquired in an area of high prevalence of PPNG (e.g. SE Asia, NSW, Victoria), or where

the patient is hypersensitive to penicillin. If these criteria are not applicable then the following regimen may be used

amoxycillin 3 g orally, with probenecid 1 g orally, both as a single dose
TOGETHER WITH
doxycycline 100 mg orally, 12-hourly for 10 days

Patients subsequently proven to have pharyngeal or ano-rectal infection should be given

ceftriaxone 250 mg intramuscularly, as a single dose

even if previously treated with another drug before culture results became available.

Sexual partners should be examined and treated appropriately.

Chlamydial and other non-gonococcal infection

doxycycline 100 mg orally, 12-hourly for 10 days

A second course, together with further investigation of the aetiology may be required if the symptoms persist or recur. Sexual partners of males with non-gonococcal urethritis should also be treated empirically to prevent recurrence in the male and to guard against chlamydial salpingitis developing in the female.

Vaginitis

Most vaginitis is not sexually transmitted. The commonest pathogen is *Candida albicans*. Bacterial vaginosis is also common. The results of Gram stain and wet preparation can be used to guide therapy.

Candida albicans

Many effective topical preparations are available (amphotericin, clotrimazole, econazole, isoconazole, miconazole, nystatin). The following regimens are two of many that have been shown to be effective.

clotrimazole vaginal tablet (500 mg), as a single dose
OR
nystatin pessaries (each containing 100,000 Units), one inserted high into the vagina once daily for 7 days. Alternatively, nystatin vaginal cream (100,000 Units per 4 g) inserted once daily for 7 days.

Bacterial vaginosis

This is the best term to describe a condition associated with malodorous vaginal discharge, paucity or absence of lactobacilli and overgrowth of *Gardnerella vaginalis*, and/or Mobiluncus species in association with other anaerobes.

metronidazole 400 mg orally, with food, twice daily for 7 days
OR
tinidazole 500 mg orally, with food, daily for 7 days
OR
amoxycillin 500 mg orally, 8-hourly for 7 days
(preferable if treatment is required in pregnancy but less effective than the above).

Trichomonas vaginalis

tinidazole or metronidazole 2g orally, with food, as a single dose
OR
clotrimazole 100 mg vaginal tablets once daily for 6 days (may be preferable if treatment is required during pregnancy).

Treatment of partner(s) is indicated as this infection is usually sexually-transmitted.

Pelvic Inflammatory Disease

Pelvic infection in females can either be sexually-acquired or result from mechanical interruption of the normal cervical barrier (e.g. post-abortal, puerperal, post-operative or in association with an intra-uterine device). Infection is usually caused by mixed pathogens taking origin from vaginal flora, including anaerobes, facultative bacteria and sometimes *Mycoplasma hominis* and *Ureaplasma urealyticum*. When sexually-acquired, infection is initiated by *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae*. Depending on the initiating factors, treatment is designed to cover this broad range of pathogens.

Sexually-acquired infection

doxycycline 100 mg orally, 12-hourly for 14 days
TOGETHER WITH EITHER
metronidazole 400 mg orally, with food, twice daily for 14 days
OR

tinidazole 500 mg orally, with food, daily for 14 days

Where penicillinase-producing *Neisseria gonorrhoeae* (which are often tetracycline-resistant) are suspected or proven metronidazole should be replaced by

amoxycillin/potassium clavulanate 500/125 mg orally, 8-hourly for 14 days

Infection not sexually-acquired

It is vital that any intra-uterine device or retained products of conception be removed at or before the start of treatment.

amoxycillin 500 mg orally, 8-hourly for 10 days
TOGETHER WITH EITHER
metronidazole 400 mg orally, with food, twice daily for 10 days
OR
tinidazole 500 mg orally, with food, daily for 10 days

Genital Ulcer

Herpes simplex causes the great majority of the genital ulceration seen our community at present. Currently available therapy is not curative, but acyclovir offers some relief or symptomatic improvement.

Herpes simplex

Primary infection

Systemic treatment is warranted in patients with severe primary herpes genitalis

acyclovir 200 mg orally, 5 times daily for 5 days

Recurrent infection

Suppressive treatment of recurrent infection is warranted only in patients who suffer very frequent recurrences (6 or more attacks in 6 months). Relapse is likely at the cessation of prophylaxis. In these cases use

acyclovir 200 mg orally, 12-hourly for 6 months

Uncommon causes

Uncommon but important causes of genital ulceration include primary syphilis, chancroid and granuloma inguinale. If any of these are suspected, referral to an STD specialist is recommended. See also p. 62-64.

Genital Lump

Warts

Warts may be removed by chemical or physical means, or by surgical removal. Treatment needs to be individualised. For small numbers of readily accessible lesions the simplest treatment is

> podophyllin 25% solution in tinc. benz. co. or absolute alcohol, applied with a cotton wool swab to each wart, and washed off in 4 hours. Application should be repeated twice weekly until the warts disappear. The normal skin surrounding the wart should be spared as much as possible.

Do not use this treatment in pregnancy, on cervical, meatal or ano-rectal warts.

The known association between genital warts and carcinoma of the cervix means that all women with warts should be referred for colposcopy. This should also apply to female partners of males with warts.

Molluscum contagiosum

These lesions are caused by a pox virus. In some cases, lesions may resolve spontaneously. The simplest treatment is to

> deroof aseptically with a needle or sharp, pointed stick, and express contents

Alternative treatments as suggested for warts are also suitable.

Genital Itch

Scabies

> lindane (gamma benzene hexachloride) 1% lotion, applied to the whole body from the neck down, left for 24 hours and then thoroughly removed by showering. Benzyl benzoate 25% is preferred in children.

Underwear and bedclothes should be well washed. Treatment may be repeated at one week.

Pubic lice

lindane, as for scabies, but applied only to the affected area
OR
pyrethrins/piperonyl butoxide foam or shampoo, applied to the affected area, left overnight, and thoroughly washed off the next day.

Underwear and bedclothes should be well washed. Treatment may be repeated at one week.

NON-SURGICAL ANTIBIOTIC PROPHYLAXIS

Prevention of recurrent rheumatic fever

Continuous antimicrobial prophylaxis is recommended for patients with a well-documented history of rheumatic fever.

phenoxymethylpenicillin 250 mg orally, twice daily for some years

If patient compliance is likely to be poor, long-acting benzathine penicillin 900 mg intramuscularly, at intervals of 3 to 4 weeks, is an effective alternative. A possible disadvantage of benzathine penicillin is that any allergic response is likely to be protracted.

For patients hypersensitive to penicillin

erythromycin 250 mg orally, twice daily

Prevention of endocarditis or infection of prosthetic implants

The case for antibiotic prophylaxis in patients with valvular heart disease, prosthetic valve implants and certain cardiac abnormalities (e.g. mitral valve prolapse with murmur) undergoing procedures that may cause transient bacteraemia is accepted, although not proven. For other implants, such as total hip replacement, the evidence supporting prophylaxis is even less definitive. However, if the patient is immunosuppressed, extensive surgery is required or established infection is present, then prophylaxis should be administered. The

recommendations that follow call for fewer doses than previously, a trend supported by many authorities.

Dental procedures, oral surgery or upper respiratory tract surgery

If the patient is NOT receiving long-term penicillin

amoxycillin 3 g orally, 1 hour before the procedure

For patients hypersensitive to penicillin or patients receiving long-term penicillin

erythromycin 1.5 g orally, 1 to 2 hours before the procedure, followed by 500 mg orally, 6 hours later

For more complicated situations see p. 69

NOTES

NOTES

METHODS OF ADMINISTRATION OF INTRAVENOUS ANTIMICROBIALS

The slow intravenous injection of antibiotics (over 1 to 2 minutes at a minimum) is an acceptable method of administration of most antibiotics (slow bolus). However, this method may produce transiently high blood levels of antibiotics that could possibly be toxic and may also predispose to thrombophlebitis. In these situations, a slow infusion via a burette or piggyback container is preferred (infusion) remembering that this method involves greater expense and may be complicated by factors such as drug stability and fluid restriction. When in doubt as to the best method of administration. slow infusion offers greater safeguards.

The compatibility with both intravenous fluids and with other drugs should always be checked, as should the stability of the antibiotic. Sources of information listed on page 13 may be utilised as well as the product literature included with the drug.

SLOW BOLUS	Reconstitute with or dilute to 10 to 20 mL of Water for Injection. Inject slowly over 1 to 2 minutes (at a minimum).
INFUSION	Reconstitute with Water for Injection and dilute in 50 to 100 mL of compatible infusion fluid in a burette or by piggyback container and infuse over 30 minutes.

Antibiotic	Recommended Method of Administration	Comments
Acyclovir	Infuse over 1 hour. The concentration of the solution must not exceed 5 mg/ml (e.g. 500 mg/100 mL)	Do not refrigerate. Stable for at least 12 hours at room temperature.
Amikacin	Infusion	
(Amoxy)ampicillin	Slow bolus Infusion for doses 2 g or greater	Limited stability, especially in dextrose solutions. Use within 2 hours.
Amphotericin	Powder to be reconstituted only with Water for Injection. Dilute only in Glucose 5%, and infuse over 6 hours.	Infusion fluid needs to be buffered at pH 4.2 or higher. (pH of commercially available Glucose 5% is usually 4.2). Solution concentration not to exceed 0.1 mg/mL (50 mg/500 mL). Stable for 6 hours.
Azlocillin	Slow bolus Infusion if the solution concentration is greater than 10% (2 g/20 mL, 5 g/50 mL)	Stable for 6 hours.

SLOW BOLUS Reconstitute with or dilute to 10 to 20 mL of Water for Injection. Inject slowly over 1 to 2 minutes (at a minimum).

INFUSION · Reconstitute with Water for Injection and dilute in 50 to 100 mL of compatible infusion fluid in a burette or by piggyback container and infuse over 30 minutes.

Antibiotic	Recommended Method of Administration	Comments
Aztreonam	Slow bolus Infusion. Use a solution not exceeding a concentration of 2% (1 g/50 mL, 2 g/100 mL)	
Benzylpenicillin	Slow bolus Infusion for doses greater than 2 g	Stability is 8 hours in Normal Saline or Hartmanns, 4 hours in glucose solutions.
Cefotaxime	Slow bolus Infusion for doses greater than 2 g	
Cefoxitin	Slow bolus Infusion for doses greater than 2 g	
Ceftazidime	Slow bolus Infusion for doses 2 g or greater	Care needed, see product literature. Carbon dioxide release produces positive pressure in vial.
Ceftriaxone	Slow bolus Infusion for doses 2 g or greater	Dilute with 10 mL Water for Injection for each gram.

SLOW BOLUS Reconstitute with or dilute to 10 to 20 mL of Water for Injection. Inject slowly over 1 to 2 minutes (at a minimum).

INFUSION Reconstitute with Water for Injection and dilute in 50 to 100 mL of compatible infusion fluid in a burette or by piggyback container and infuse over 30 minutes.

Antibiotic	Recommended Method of Administration		Comments
Cephalothin	Slow bolus Infusion for doses greater than 2 g		Dilute with 10 mL Water for Injection for each gram.
Cephamandole	Slow bolus Infusion for doses greater than 2 g		Dilute with 10 mL Water for Injection for each gram.
Cephazolin	Slow bolus Infusion for doses greater than 2 g		
Chloramphenicol	Slow bolus Infusion for doses greater than 1.2 g		Solution concentration should not exceed 100 mg/mL.
Clindamycin	Infusion only		
Co-trimoxazole	Dose Volume 5 mL 10 mL 15 mL	Dilution Volume 100 mL 250 mL 500 mL	Not to be used undiluted. IV lines should be flushed with Normal Saline before and after administration. Do not refrigerate. Use immediately. Infuse over 1 to 1.5 hours.
Doxycycline	Infusion only		Infusion solution concentration should not exceed 0.5 mg/mL (100 mg/200 mL).

SLOW BOLUS Reconstitute with or dilute to 10 to 20 mL of Water for Injection. Inject slowly over 1 to 2 minutes (at a minimum).

INFUSION Reconstitute with Water for Injection and dilute in 50 to 100 mL of compatible infusion fluid in a burette or by piggyback container and infuse over 30 minutes.

Antibiotic	Recommended Method of Administration	Comments
Erythromycin	Slow bolus Infusion for doses greater than 1 g	Reconstitute powder ONLY with Water for Injection.
Flucloxacillin	Slow bolus Infusion for doses greater than 2 g	
Flucytosine	Supplied as 2.5 g/250 mL IV solution. Infuse over 20 to 30 minutes.	
Fusidic acid (see Sodium Fusidate)		
Gentamicin	Slow bolus or Infusion	
Imipenem/Cilastatin	Infusion only. Doses of 1 g or greater should be infused over 40 to 60 minutes in 100 to 250 mL fluid.	Use within 4 hours at room temperature.
Lincomycin	Infusion	

SLOW BOLUS	Reconstitute with or dilute to 10 to 20 mL of Water for Injection. Inject slowly over 1 to 2 minutes (at a minimum).
INFUSION	Reconstitute with Water for Injection and dilute in 50 to 100 mL of compatible infusion fluid in a burette or by piggyback container and infuse over 30 minutes.

Antibiotic	Recommended Method of Administration	Comments
Metronidazole	Supplied as 500 mg/100 mL IV solution. Infuse over a minimum of 30 minutes.	
Netilmicin	Slow bolus or Infusion	
Penicillin (see Benzylpenicillin)		
Piperacillin	Slow bolus or Infusion (particularly for doses greater than 4 g)	Dilute with 5 mL Water for Injection for each gram. Each gram contains 2 mmol of sodium.
Rifampicin	Dissolve in solvent supplied and further dilute to 500 mL. Infuse over 1 to 3 hours.	Use within 6 hours.
Rolitetracycline	Slow bolus or Infusion	
Sodium Fusidate	Reconstitute with diluent provided. Dilute in 250 to 500 mL of Normal Saline and infuse over 2 to 4 hours.	

SLOW BOLUS Reconstitute with or dilute to 10 to 20 mL of Water for Injection. Inject slowly over 1 to 2 minutes (at a minimum).

INFUSION Reconstitute with Water for Injection and dilute in 50 to 100 mL of compatible infusion fluid in a burette or by piggyback container and infuse over 30 minutes.

Antibiotic	Recommended Method of Administration	Comments
Ticarcillin	Slow bolus or Infusion for doses greater than 3 g	Dilute with at least 4 mL Water for Injection for each gram. Each gram contains 6 mmol of sodium.
Ticarcillin/ Potassium Clavulanate	Infusion	Each gram contains 6 mmol of sodium.
Tobramycin	Slow bolus or Infusion	
Vancomycin	Infusion ONLY. Infuse over at least 60 minutes.	Reconstitute with Water for Injection.

SLOW BOLUS Reconstitute with or dilute to 10 to 20 mL of Water for Injection. Inject slowly over 1 to 2 minutes (at a minimum).

INFUSION Reconstitute with Water for Injection and dilute in 50 to 100 mL of compatible infusion fluid in a burette or by piggyback container and infuse over 30 minutes.

MICROORGANISM/ANTIMICROBIAL CHART

ANTIBIOTICS most likely to be clinically effective against ORGANISM groups listed, pending availability of sensitivity and identification results.

KEY:
1 = first choice
2 = second choice
3 = not usually recommended*
R = relatively inactive or organism likely to be resistant

	Penicillin	(Amoxy)ampicillin	Ticarcillin	(Flu)cloxacillin	Cephalothin/cephalexin	Cefoxitin	Tetracycline	Co-trimoxazole	Erythromycin	Clindamycin	Metronidazole/tinidazole	Gentamicin/Tobramycin	Vancomycin
Staphylococci (likely to be methicillin-sensitive)	3	3	3	1	1	3	3	3	2	2	R	3	3
Staphylococci (likely to be methicillin-resistant)	R	R	R	R	R	R	R	R	R	R	R	R	1
Streptococci (non-enterococcal strains)	1	2	3	4	2	3	3	2	2	3	R	R	2
Streptococci (enterococci & *Strep.faecalis*)	1	1	3	R	R	R	2	3	2	3	R	R	2
Aerobic Gram-negative bacilli	R	2	2	R	2	2	3	1	R	R	R	1	R
Pseudomonas aeruginosa	R	R	1	R	R	R	R	R	R	R	R	1	R
Anaerobic Gram-negative bacilli	3	3	2	R	3	2	3	3	3	1	1	R	R
Anaerobic Gram-positive bacilli/cocci	1	2	3	3	2	2	3	3	2	2	1	R	3
Haemophilus sp. (not in meningitis)	2	1	3	R	R	R	2	1	3	3	R	3	R

* Not usually recommended either because drug is less active against stated organism(s), resistance is likely, clinical efficacy is reduced in comparison with first or second choice drugs, or the drug is expensive or toxic in comparison with alternatives.

This table is a simplified guide to assist in the empirical choice of antibiotic therapy and as such should be used in conjunction with recommendations made under specific sections of the Guidelines.

MONITORING ANTIMICROBIAL BLOOD LEVELS

This may be undertaken to minimise toxicity and/or to ensure that adequate levels are attained in relation to a target set from microbiological data or occasionally to assess compliance with oral therapy.

Monitoring for toxicity is applicable to:

Drug	Toxic Level mmol/l	Toxic Level (ug/ml, mg/l)	Need to Monitor
Gentamicin (a)		(>2) trough (b) (>10) peak (b)	Routinely at least once during a course of therapy
Tobramycin	>4 >17	(>2) trough (b) (>10) peak (b)	
Amikacin	>8.5 >34	(>5) trough (b) (>20) peak (b)	
Vancomycin	>7 >27.5	(>10) trough (b) (>40) peak (b)	
Co-trimoxazole Sulphamethoxazole Trimethoprim	>450 >10	(>115) peak (>3) peak	Occasionally in the presence of renal impairment
Flucytosine	>600	(>80) peak	In renal impairment e.g. due to amphotericin toxicity
Chloramphenicol	>60	(>20) peak	Routinely in the newborn
Penicillins		(c) peak	With high dose and renal impairment

(a) Gentamicin is a mixture of related substances with different molecular weights, thus quoting concentrations in terms of umol/l is inappropriate.

(b) Trough levels correlate better with toxicity; transiently high peak levels are less dangerous. Trough levels should be sampled immediately before the next dose is administered. Peak levels should normally be sampled 30 minutes after the completion of administration of the dose or as instructed by the laboratory.

(c) CNS toxicity depends on CSF levels and the relationship of this to blood levels varies. Meningeal inflammation and use of probenecid increase CSF levels for a given plasma level.

PAEDIATRIC DOSES OF ANTIMICROBIAL AGENTS

This table contains recommended doses only of currently available antimicrobials which are used systemically. The table also only refers to children older than 4 weeks, i.e. dosage recommendations for neonates are not included.

Young children have a large volume of distribution of many antibiotics in the body; this means that, in order to achieve satisfactory serum concentrations, the larger doses based on body weight are given, compared to those recommended for adults on the same basis. Older children and teenagers are pharmacologically more like adults; if standard paediatric formulas to calculate drug dosage are used, overdosage can result. It is important that dosages calculated from data in this table do not exceed those recommended for adults.

PAEDIATRIC DOSES

Antimicrobial & Route of Administration	Usual Dose mg/kg/24hr	Severe Infections Maximal Dose mg/kg/24 hour
Penicillins and Related Drugs		
Benzylpenicillin IM or IV	60-120 mg (100,000-200,000 Units) in 4 or 6 divided doses	150 mg (250,000 Units) in 4 or 6 divided doses
Procaine penicillin IM	50 mg (50,000 Units) once daily	Not applicable
Benzathine penicillin IM	Available in 450 mg (600,000 Units) vials. Administered only IM. Children older than two months, those 2-6 years of age and those over 6 years should be given 1/2 vial, 3/4 vial and one vial, respectively once every 2 to 3 weeks	
Phenoxymethyl-penicillin (Penicillin V) O	25-50 mg in 4 divided doses	Not applicable
Ampicillin O IM IV	25-75 mg in 4 divided doses	150 mg in 4 divided doses
Amoxycillin O IM IV	25-75 mg in 3 divided doses	150 mg in 4 divided doses
Amoxycillin/ potassium clavulanate O	20/5 - 40/10 in 3 divided doses	Not applicable
Aztreonam IV	90 mg in 3 divided doses	120 mg in 4 divided doses
Imipenem/cilastatin IV	60 mg* in 4 divided doses	100 mg in 4 divided doses
(Flu)cloxacillin O IM IV	50-100 mg in 4 divided doses	200 mg in 4 or 6 divided doses
Ticarcillin IV	150-300 mg in 4 divided doses	300-400 mg in 4 to 6 divided doses
Ticarcillin/potassium clavulanate IV	200-300 mg# in 4 to 6 divided doses	300-400 mg in 4 to 6 divided doses

Antimicrobial & Route of Administration	Usual dose mg/kg/24hr	Severe Infections Maximal Dose mg/kg/24 hour
Piperacillin IM IV	100-150 mg in 4 to 6 divided doses	300 mg in 4 to 6 divided doses
Azlocillin IM IV	100-300 mg in 4 divided doses	450 mg in 4 to 6 divided doses
Cephalosporins		
Cephalothin IM IV	50-100 mg in 4 divided doses	200 mg in 4 divided doses
Cephalexin O	25-50 mg in 4 divided doses	Not applicable
Cephazolin IM IV	25-50 mg in 3 or 4 divided doses	100 mg in 4 divided doses
Cefaclor O	40-50 mg in 3 or 4 divided doses	Not applicable
Cephamandole IM IV	50-100 mg in 3 or 4 divided doses	150 mg in 4 divided doses
Cefoxitin IM IV	50-100 mg in 3 or 4 divided doses	150 mg in 4 divided doses
Cefotaxime IM IV	100-150 mg in 3 or 4 divided doses	150-200 mg in 4 divided doses
Ceftazidime IV	50 mg in 3 divided doses	100 mg in 3 divided doses
Ceftriaxone IM IV	50-100 mg in 1 or 2 divided doses	100 mg in 2 divided doses
Aminoglycosides		
Streptomycin IM IV	20-40 mg in 1 or 2 divided doses	40 mg in 1 or 2 divided doses
Gentamicin IM IV	7.5 mg in 3 divided doses	Up to 12 mg in 3 divided doses
Tobramycin IM IV	4.5 mg in 3 or 4 divided doses	7.5 mg in 3 or 4 divided doses

* Refers to imipenem content
# Refers to ticarcillin content

Antimicrobial & Route of Administration	Usual dose mg/kg/24hr	Severe Infections Maximal Dose mg/kg/24 hour
Amikacin IM IV	15 mg in 2 divided doses	24 mg in 3 divided doses
Netilmicin IM IV	6 mg in 3 divided doses	7.5 mg in 3 divided doses
Other Antibacterial Antibiotics		
Chloramphenicol O IM IV	50 mg in 4 divided doses	80-100 mg in 4 divided doses
Clindamycin O IM IV	8-16 mg in 3 or 4 divided doses	16-20 mg in 3 or 4 divided doses
Fusidate Sodium O IV	20-40 mg in 3 divided doses	50 mg in 3 divided doses
Erythromycin O IM IV	25-50 mg in 3 or 4 divided doses	100-150 mg in 4 divided doses
Tetracycyline O	25 mg in 4 divided doses (usually only use in children over age of 7 years)	50 mg etc
Doxycycline O IV	2 mg in 1 or 2 divided doses (also avoid in children younger than 7 years)	4 mg in 1 or 2 divided doses (also avoid in children younger than 7 years)
Vancomycin IV	30 mg in 2 or 4 divided doses	40-60 mg in 4 divided doses
Synthetic Antibacterial Drugs		
Sulphamethizole O	50-100 mg in 3 or 4 divided doses	Not applicable
Ciprofloxacin	Not recommended for children	
Co-trimoxazole O IV	sulphamethoxazole/ trimethoprim 30/6 mg in 2 divided doses	e.g. for Pneumo-cystis carinii inf 100/20 mg in 4 divided doses

Antimicrobial & Route of Administration	Usual dose mg/kg/24hr	Severe Infections Maximal Dose mg/kg/24 hour
Nalidixic Acid O	50 mg in 4 divided doses	Not applicable
Norfloxacin O	Not recommended for children	
Nitrofurantoin O	5-7 mg in 4 divided doses	Not applicable
Metronidazole (for anaerobic infections only) O IV	20-30 mg in 3 divided doses	30 mg in 3 divided doses
Drugs Mainly For Tuberculosis		
Isoniazid O	10 mg - one dose each morning	Up to 20 mg in 1-2 divided doses
Rifampicin O IV	10 mg in 1 or 2 divided doses	Up to 20 mg in 1-2 divided doses
Para-amino salicyclic Acid O	150 mg in 1 or 2 doses	As for usual dose
Ethambutol (Maintenance treatment) O	15 mg in 1 dose each morning	
Pyrazinamide O	40 mg in 2 or 3 doses	
Antifungal Drugs		
Amphotericin (This is maximal dose. Therapy commences with 0.1 mg test dose daily and this is gradually increased to maximal dose) IV	1.0 mg as a 5-6 hr daily IV infusion	1.5 mg as a 5-6 hr daily IV infusion
Flucytosine O IV	100-150 mg in 4 divided doses	150-200 mg in 4 divided doses
Miconazole IV	20 mg in 3 divided doses	40 mg in 3 divided doses

Antimicrobial & Route of Administration	Usual dose mg/kg/24hr	Severe Infections Maximal Dose mg/kg/24 hour
Ketoconazole O	30 mg in single daily dose	Not applicable
Griseofulvin O	10-15 mg in 2 divided doses	
Antiviral Drugs		
Vidarabine IV	10 mg as continuous infusion over 12 hr	15 mg as IV infusion over 12 hr
Acyclovir IV	15 mg in 3 divided doses	30 mg in 3 divided doses

INDEX

NOTES

NOTES

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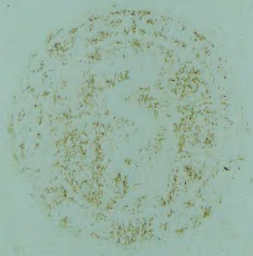
NOTES



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